

Inhibitors and UnCouplers of Oxidative Phosphorylation

Ability to harness energy from external sources and utilize it for biological work is characteristic of all living organisms. Phototrophs harvest the energy of light (Plants). Chemotrophs harvest energy from oxidation of fuel molecules. The oxidation of foodstuffs occurs in three stages.

Oxidative Stages of Food Stuff:

1. Primary Metabolism:

In the first stage, DIGESTION in the gastrointestinal tract converts the macromolecules into small units. For example, proteins are digested to amino acids and Polysaccharides are into monosaccharides, etc. This is called Primary Metabolism.

2. Secondary Metabolism:

The products of primary metabolism are absorbed, catabolised to smaller components and ultimately oxidised to carbondioxide. The reducing equalents mainly generated in the mitochondria by the final common oxidative pathway, citric acid cycle. In the final process, NADH and FADH₂ are generated. This is called Secondary Metabolism.

3. Tertiary Metabolism (or) Internal Metabolism:

The secondary metabolism products Reducing equivalents (NAHD and FADH₂) enter into the electron transport chain (ETC, Respiratory chain), where energy is released. This is called Tertiary metabolism (or) Internal Metabolism (or) Cellular Respiration.

Respiratory Inhibitors:

The ETC chain contains 4 complexes (I, II, III and IV) which participate in the transfer of electrons. In general, it may be stated that the structural integrity of these complexes appears essential for its interaction with most inhibitors, since the soluble, phospholipid free enzymes do not exhibit the characteristic inhibitory pattern. Components in Electron Transport Chain system in Mitochondria

Electron transport chain mechanism.

The following compounds inhibit both electron transport and oxidative phosphorylation.

Inhibitors of Electron Transport:

These are the inhibitors that arrest respiration by combining with members of the respiratory chain, rather than with the enzymes that may be involved in coupling respiration with ATP synthesis. They appear to act at 3 loci that may be identical to the energy transfer sites I, II and III. The given below are the inhibitors of Electron transport chain.

1. Rotenone:

It is the non-toxic inhibitors of Electron transport chain.

These compound extracted from roots of tropical plant *Derris elliptica* and *Lonchocarpus nicou*.

It binds at Complex I between **Fe-S protein** and **Ubiquinone**.

This is non-toxic to mammals because poorly absorbed. Shows toxic effect in fishes.

