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Biological Oxidation:

Oxidation process or reaction in biological system / cell is called biological oxidation.

During this process the, high energy compound converted in to low energy compound & their is liberation of energy in form of heat which is then converted in to chemical energy (or ATP)

Enzymes of biological oxidation

Enzymes: Oxidoreductase class

- → oxidase
- → Dehydrogenases
- → Hydroperoxidase
- → oxygenases

Co enzymes:

- → NAD^+
- → $NADP^+$
- → FMN
- → FAD

Oxidases: enzymes which catalyse removal of Hydrogen using oxygen as hydrogen acceptor

$$MH_2 + O \longrightarrow M^+ + H_2O$$

Ex

- Cytochrome oxidases
- L-amino acid oxidases
- Xanthine oxidases

Teacher's Signature : ....

② **Dehydrogenases**: Enzyme which catalyse removal of Hydrogen without using oxygen as hydrogen acceptor.

The hydrogen is accepted by different coenzymes

$$MH_2 \xrightarrow{\text{dehydrogenase}} M^+$$

$NAD^+/NADP^+ \rightarrow NADH + H^+/NADPH + H^+$

ex of coenzymes
NAD^+ or $NADP^+$ (Derived from Vit B_3)
FMN or FAD (Vit B_2)

→ NAD^+ linked coenzyme are involved in catabolic pathways such as Glycolysis, TCA cycles & produce energy

→ $NADP^+$ linked coenzyme are involved in anabolic pathways such as fatty acid synthesis, cholesterol biosynthesis.
$NADP^+$ linked coenzyme do not produce energy

$$MH_2 \longrightarrow M^+$$

$FAD/FMN \rightarrow FADH_2/FMNH_2$

examples of FMN/FAD linked dehydrogenase
TCA → Succinate dehydrogenase
β-oxidation → acyl CoA dehydrogenase

③ ~~Oxygenases~~ **Hydroperoxidases**: catalyze reduction of H_2O_2 to H_2O

$$H_2O_2 \xrightarrow{\text{Peroxidases}} H_2O + \dot{O}$$

$$H_2O_2 \xrightarrow{\text{Catalase}} H_2O + O_2$$

Example
peroxidases
Catalases

(4) **Oxygenases:** Catalyse addition of oxygen in the molecules without any energy production

Types

→ Monooxygenase
- Insert only one oxygen & other reduce to H_2O

$M-H \xrightarrow{O_2} M-OH + H_2O$

Example: Phenylalanine hydroxylase

$\text{Phenylalanine} \xrightarrow{O_2} \text{Tyrosine} + H_2O$

→ Dioxygenases
- Insert 2 atom of oxygen

$M{<}^{H}_{H} \xrightarrow{O_2} M{<}^{OH}_{OH}$

example
- → Cycloxygenase
- → Tryptophan dioxygenase
- Homogentisate oxidase

$\text{homogentisate} \xrightarrow[\text{O}_2 \quad \text{Vit C}]{} \text{Malylacetoacetate}$

Electron transport chain (ETC) or Respiratory Chain

Food oxidation ⟶ $NADH^{+}/FADH_2$

$NADH/FADH_2 \xrightarrow{ETC} O_2 + ATP$ (energy)

ETC : Location: Inner mitochondrial ~~matrix~~ membrane

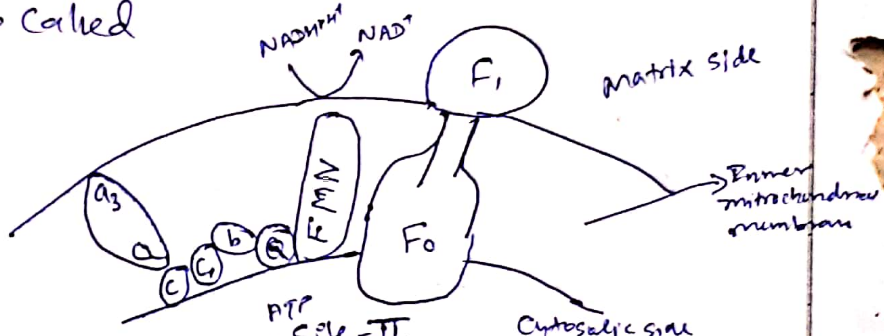
Component of ETC : —

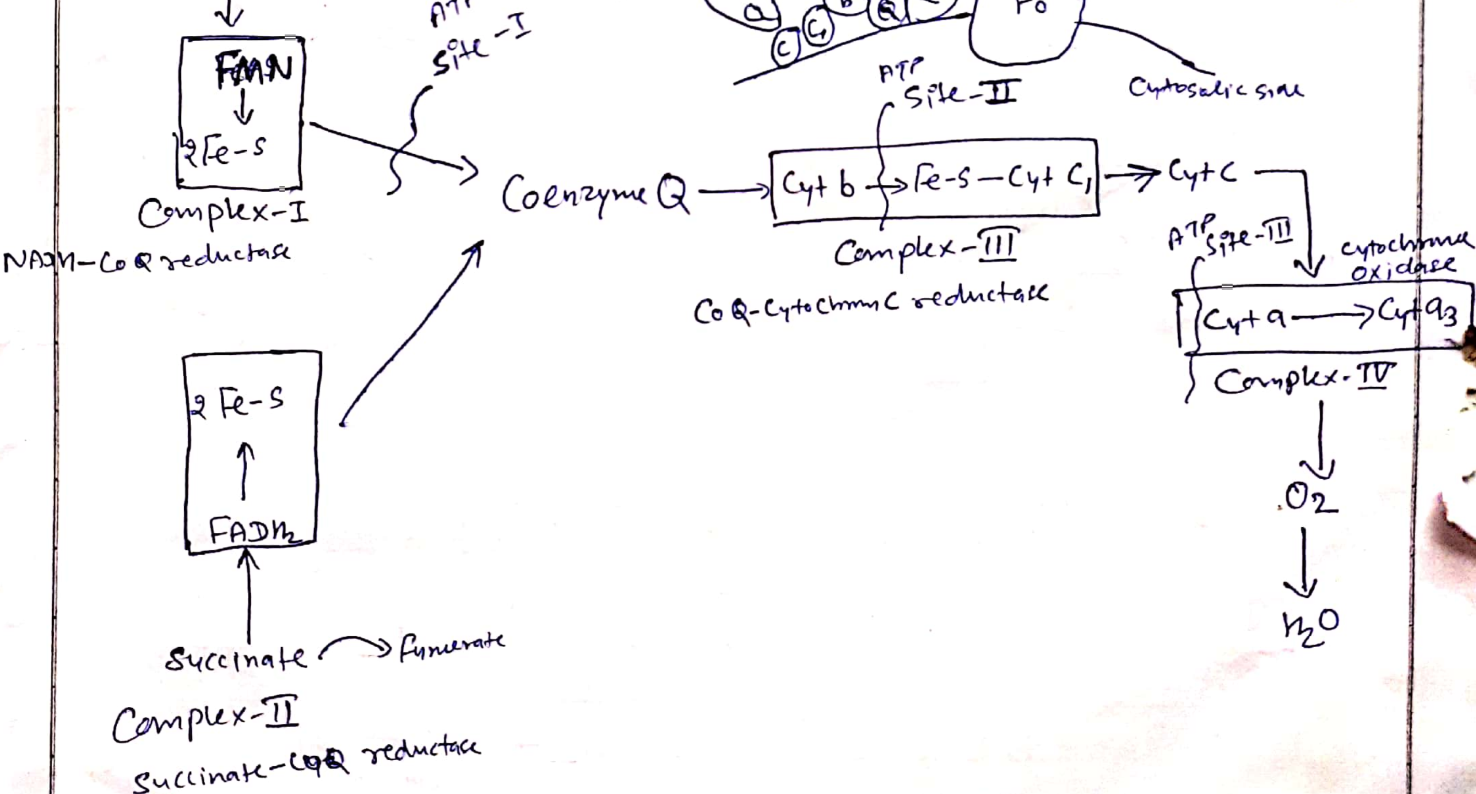
- NAD^+
- FMN/FAD
- Coenzyme Q. / Ubiquinone
- Fe-S protein associated with FMN & cytochrome b
- Cytochrome (Heme proteins) b, c_1, c, a & a_3

only Cytochrome C is water soluble

other are embided in lipid bilayer

Cytochrome aa_3 = also called cytochrome oxidase





ELECTRON TRANSPORT CHAIN (ETC) OR RESPIRATORY CHAIN

The final steps in the overall oxidation of food stuffs (carbohydrate, fat and amino acids) result in formation of NADH and $FADH_2$.

The electron transport chain (ETC) oxidizes NADH and $FADH_2$ by transferring electrons (reducing equivalents) by a series of oxidation reduction reactions to O_2, the terminal electron acceptor. In the presence of O_2, the ETC converts reducing equivalents into energy, (ATP) by oxidative phosphorylation.

Localization of the Electron Transport Chain

The electron transport chain is present in the ***inner mitochondrial membrane (Figure 10.1).*** The enzymes of the electron transport chain are embedded in the inner membrane.

Components of the Electron Transport Chain

The major components of the electron transport chain include:

- Nicotinamide adenine dinucleotide (NAD^+).
- Flavin mononucleotide (FMN) and Flavin adenine dinucleotide (FAD).
- Ubiquinone or coenzyme Q.
- The ***iron-sulfur (Fe-S) protein*** associated with FMN and cytochrome b.
- Cytochromes (hemeproteins): b, c_1, c, a and a_3. Of these, only cytochrome c is water soluble and easily diffusible, whereas cytochromes b, c_1, a and a_3 are lipid soluble and therefore, are fixed components of

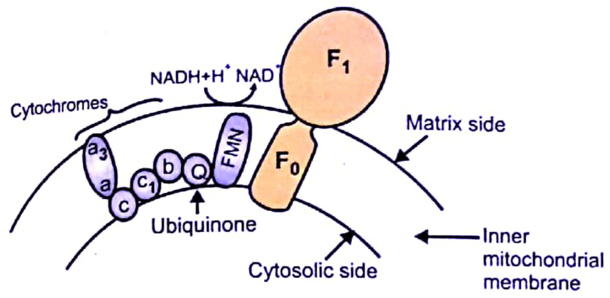


Figure 10.1: Structural organization of components of respiratory chain and F_oF_1 ATPase in the mitochondrial membrane

the membrane. Cytochrome aa_3 are also called **cytochrome oxidase;** and are **copper containing hemeproteins.**

Except coenzyme Q, all members of this chain are proteins. Coenzyme Q (CoQ) is a fat soluble quinone (ubiquinone) and is a constituent of mitochondrial lipids.

Structural Organization of Components of Electron Transport Chain

The mitochondrial electron carriers are organized into four complexes (complex I to IV) that catalyze oxidation-reduction reactions of the electron transport chain **(Figure 10.2).**

- **Complex I, NADH- CoQ reductase,** catalyzes the transfer of electrons from NADH to coenzyme Q (CoQ).
- **Complex II, Succinate-CoQ reductase,** transfers electrons from succinate to coenzyme Q.
- **Complex III, CoQ- Cytochrome c reductase,** transfers electrons from CoQ to cytochrome c.
- **Complex IV, Cyctochrome oxidase,** transfers electrons from cytochrome c to O_2.

Components of the respiratory chain are arranged in order of increasing redox potential **(Table 10.1).** Reducing equivalents flow through the chain from the components **of more negative redox potential to the components of more positive redox potential.**

Reactions of Electron Transport Chain

The following sequence of reactions occurs in the transfer of electrons from substrate to the ultimate acceptor oxygen **(Figure 10.3).**

1. NAD^+ is reduced to NADH by various dehydrogenases which remove two hydrogen atoms from their metabolite (MH_2) and get oxidized to M. In this oxidation reduction reaction, one hydrogen atom is accepted by NAD^+ to form NADH, while the second proton (H^+) is released into the aqueous medium.
2. The reduced NADH is oxidized by an enzyme **NADH dehydrogenase.** This enzyme contains **coenzyme FMN.** The coenzyme FMN accepts two electrons ($2e^-$) and a proton (H^+) from NADH and a free H^+ from the aqueous medium to form $FMNH_2$.
3. In addition to FMN, NADH dehydrogenase also consists of **Fe-S proteins,** which accepts only electron from $FMNH_2$. Thus two Fe-S protein molecules accept two electrons from one $FMNH_2$ molecule with release of two protons ($2H^+$) into the medium and $FMNH_2$ gets oxidized to FMN.
4. CoQ accepts two electrons from two Fe-S protein molecules and two protons ($2H^+$) from the medium

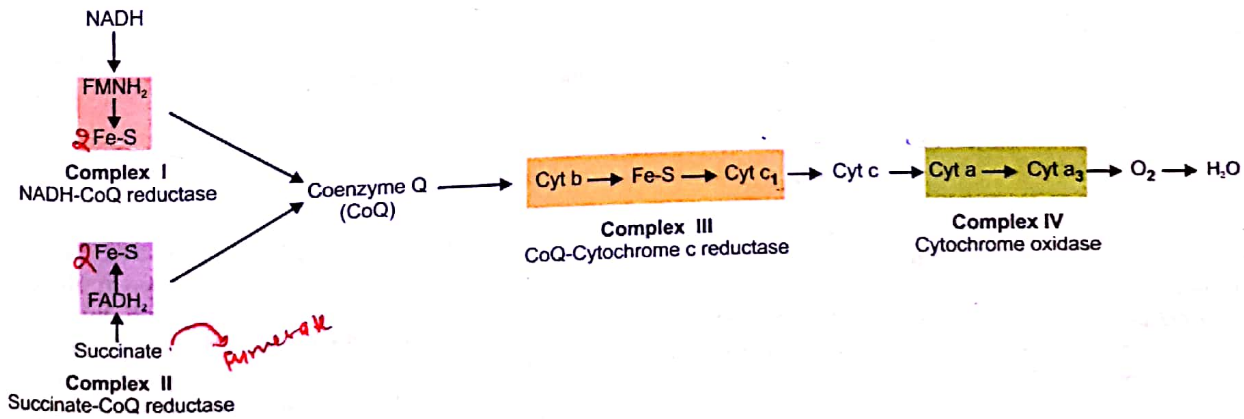


Figure 10.2: The electron transport complexes

Table 10.1: The redox potential Eo' of redox couples of components of electron transport chain

Redox couple		*components of electron transport chain*	*Redox potential Eo' in volt*
$2H^+ + 2e^-$	→	H_2	– 0.41
$NAD + H^+ + 2e^-$	→	NADH	– 0.32
$FMN + 2H^+ + 2e^-$	→	$FMNH_2$	– 0.32
Ubiquinone $+2H^+ + 2e^-$	→	Ubiquinol	+ 0.04
Cytochrome b (ox) + e^-	→	Cytochrome b (red)	+ 0.07
Cytochrome c_1 (ox) + e^-	→	Cytochrome c_1 (red)	+ 0.23
Cytochrome c (ox) + e^-	→	Cytochrome c (red)	+ 0.25
Cytochrome a (ox) + e^-	→	Cytochrome a (red)	+ 0.29
Cytochrome a_3 (ox) + e^-	→	Cytochrome a_3 (red)	+ 0.55
$1/2O_2 + 2H^+ + 2e^-$	→	H_2O	+ 0.82

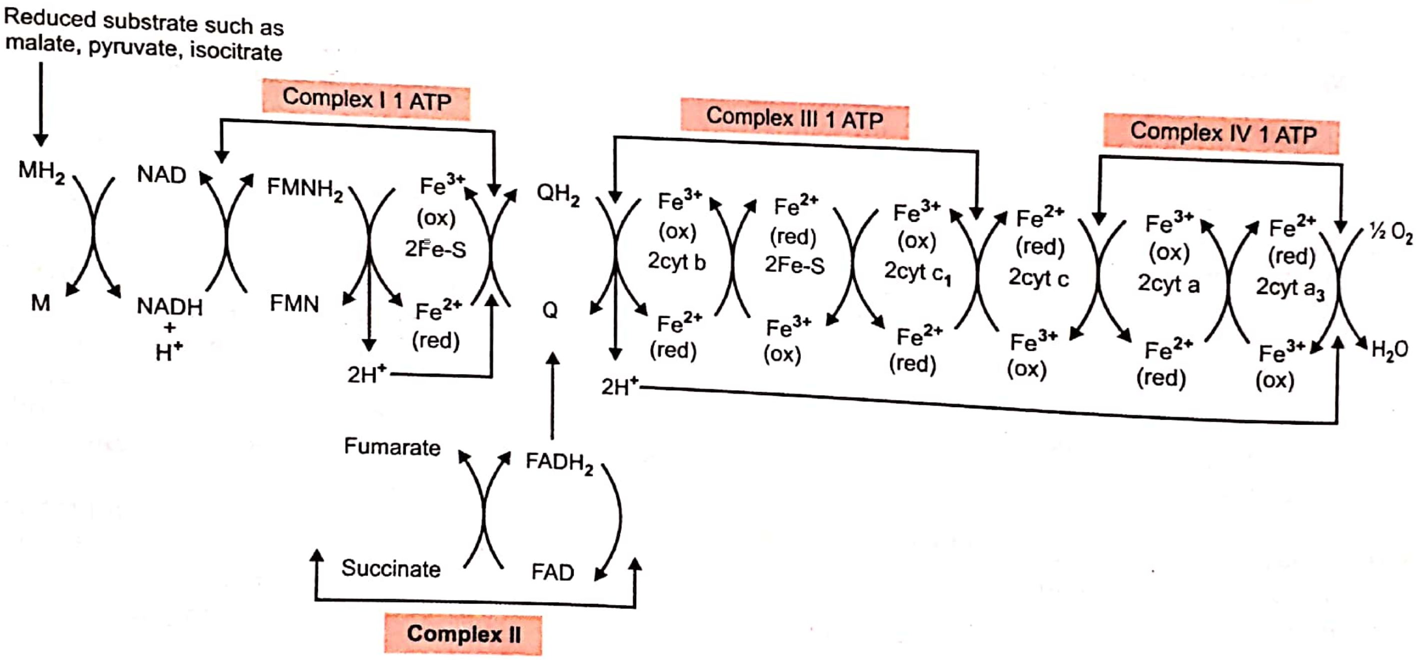


Figure 10.3: Electron transport chain

to get reduced to $CoQH_2$. CoQ also collects reducing equivalents from $FADH_2$ formed by FAD-linked dehydrogenases.

5. Beyond CoQ, oxidation reduction process occurs by removal of electrons with the help of **cytochromes.** Cytochromes accept only electrons from coenzyme QH_2 with the release of $2H^+$ in the medium. As a cytochrome can accept only one electron, $CoQH_2$ transfers its two electrons to two molecules of cytochrome b, c_1 c, a and a_3 sequentially.
6. The last cytochrome complex is cytochrome oxidase (cyt aa_3) which passes electrons from cytochrome c to molecular oxygen. Each oxygen atom accepts two electrons from cytochrome a_3 and two protons from the medium and a molecule of water results.

> The reduction of O_2 by cytochrome oxidase reaction accounts for the production of about **300 ml of water/day.** This water is called ***metabolic water.***

Formation of ATP

During the transfer of electrons through the electron transport chain, energy is produced. This energy is coupled to the formation of ATP molecules by phosphorylation of ADP by an enzyme **$F_0 F_1$ ATPase.** The formation of ATP from ADP and Pi is termed **phosphorylation,** as phosphorylation is coupled with biological oxidation, the process is called ***biological oxidative phosphorylation.***

Sites of ATP Synthesis

- There are three ATP synthesizing sites of the electron transport chain, these are **(Figure 10.4)**:
  1 Oxidation of $FMNH_2$ by CoQ
  2 Oxidation of cytochrome b by cytochrome c_1
  3 Cytochrome oxidase reaction (oxidation of cytochrome a by cytochrome a_3.
- These sites provide the energy required to make ATP from ADP and Pi by an enzyme $F_0 F_1$ ATPase.
- Electrons that enter the chain through NADH pass through all three ATP synthesizing sites and thus yield three ATPs.
- However, electrons that enter the chain through $FADH_2$ pass through only two ATP synthesizing sites, as they bypass site 1, they yield two ATPs.

INHIBITORS OF ELECTRON TRANSPORT CHAIN

Inhibitors of respiratory chain may be divided into three groups.

1. Inhibitors of the electron transport chain proper
2. Inhibitors of oxidative phosphorylation (F_0F_1 ATPase)
3. Uncouplers of oxidative phosphorylation.

Inhibitors of Electron Transport Chain Proper (Figure 10.5)

Inhibitors of electron transport chain proper include, inhibitors that inhibit the flow of electrons through the respiratory chain. These inhibitors block the respiratory chain at three sites:

1. **Complex I (NADH to CoQ),** inhibited by:
   - Barbiturates such as amobarbital
   - An antibiotic piericidin A
   - The insecticide rotenone.

These inhibitors prevent the oxidation of substrates by blocking the transfer of reducing equivalents from Fe-S protein to CoQ.

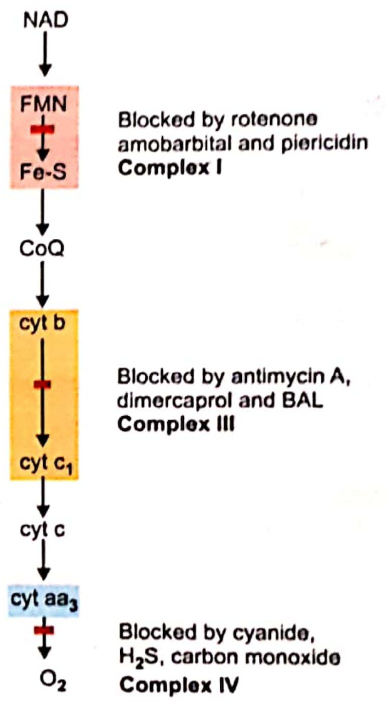


Figure 10.5: Sites of action of various inhibitors of electron transport chain

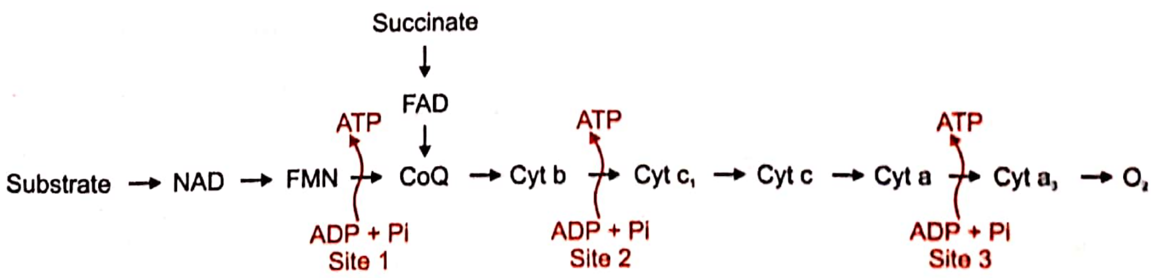


Figure 10.4: ATP synthesizing sites of electron transport chain

2. **Complex III (cytochrome b to cytochrome c_1),** inhibited by:
   - Dimercaprol
   - Antimycin A (antibiotics)
   - British antilewisite (BAL), an antidote used against war gas.

These inhibitors prevent the transfer of electrons from cytochrome b to cytochrome c_1.

3. **Complex IV (cytochrome oxidase),** inhibited by:
   - Cyanide
   - Carbon monoxide
   - H_2S.

These inhibitors prevent transfer of electrons from cyt aa_3 to molecular oxygen by inhibiting cytochrome oxidase and can therefore totally arrest respiration.

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