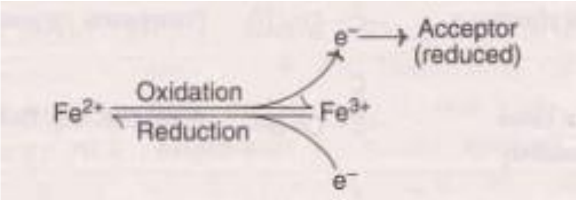
BIOCHEMISTRY- BP203T

UNIT : 1 METABOLISM OF CARBOHYDRATES

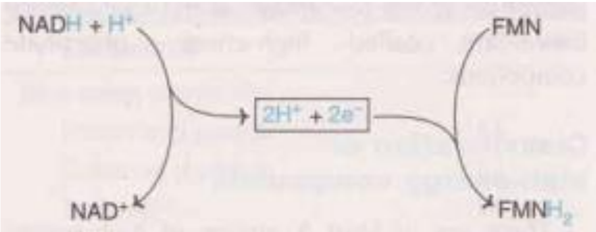
CLASS:8

TOPIC: BIOLOGICAL OXIDATION & ELECTRON TRANSPORT CHAIN

Oxidation is defined as the loss of electrons and **reduction** as the gain of electrons. This may be illustrated by the interconversion of ferrous ion (Fe2+) to ferric ion (Fe3+).



The electron lost in the oxidation is accepted by an acceptor which is said to be reduced. Thus the oxidation-reduction is a tightly coupled process.



The general principle of oxidation-reduction is applicable to biological systems also. The oxidation of NADH to NAD+ coupled with the reduction of FMN to FMNH2 is illustrated

In the above illustration, there are two redox pairs NADH/NAD+ and FMN/FMNH2. The redox pairs differ in their tendency to lose or gain electrons

Redox potential (E0)

The oxidation-reduction potential or, simply, redox potential, is a quantitative measure of the tendency of a redox pair to lose or gain electrons.

The redox pairs are assigned specific standard redox potential (E0 volts) at pH 7.0 and 25°C.

The redox potentials of some biologically important redox systems are given in Table 11.3.

The more negative redox potential represents a greater tendency (of reductant) to lose electrons.

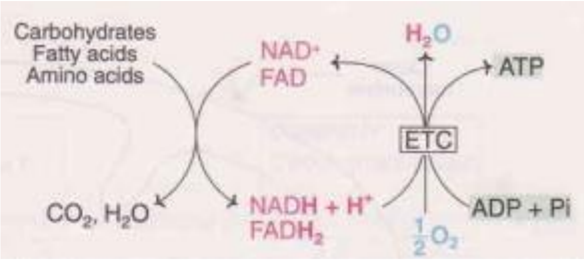
On the other hand, a more positive redox potential indicates a greater tendency (of oxidant) to accept electrons.

The electrons flow from a redox pair with more negative E0 to another redox pair with more positive E0.

The redox potential (E0) is directly related to the change in the free energy ('G°).

ELECTRON TRANSPORT CHAIN:

The energy-rich carbohydrates (particularly glucose), fatty acids and amino acids undergo a series of metabolic reactions and, finally, get oxidized to CO2 and H2O.



The reducing equivalents from various metabolic intermediates are transferred to coenzymes NAD+ and FAD to produce, respectively, NADH and FADH2.

The latter two reduced coenzymes pass through the electron transport chain (ETC) or respiratory chain and, finally, reduce oxygen to water.

The passage of electrons through the ETC is associated with the loss of free energy.

A part of this free energy is utilized to generate ATP from ADP and Pi (Fig.11.3).

Mitochondria – the powerhouses of the cell

Mitochondria are the centres for metabolic oxidative reactions to generate reduced coenzymes (NADH and FADH2), which, in turn, are utilized in ETC to liberate energy in the form of ATP.

For this reason, mitochondrion is appropriately regarded as the powerhouse of the cell.

Mitochondrial organization

The mitochondrion consists of five distinct parts.

These are the outer membrane, the inner membrane, the intermembrane space, the cristae, and the matrix (Fig.11.5).

Inner mitochondrial membrane:

The electron transport chain and ATP-synthesizing system are located on the inner mitochondrial membrane, which is a specialized structure, rich in proteins.

It is impermeable to ions (H+, K+, Na+) and small molecules (ADP, ATP).

This membrane is highly folded to form cristae.

The surface area of the inner mitochondrial membrane is greatly increased due to cristae.

The inner surface of the inner mitochondrial membrane possesses specialized particles (that look like lollipops), the phosphorylating subunits, which are the centers for ATP production.

Mitochondrial matrix:

The interior ground substance forms the matrix of mitochondria. It is rich in the enzymes responsible for the citric acid cycle, E-oxidation of fatty acids, and oxidation of amino acids.

Structural organization of the respiratory chain:

The inner mitochondrial membrane can be disrupted into five distinct respiratory or enzyme complexes, denoted as complex I, II, III, IV, and V (Fig.11.6).

Complexes I-IV are carriers of electrons, while complex V is responsible for ATP synthesis. Besides these enzyme complexes, there are certain mobile electron carriers in the respiratory chain.

These include NADH, coenzyme Q, cytochrome C, and oxygen.

Components and reactions of the electron transport chain:

Five distinct carriers participate in the electron transport chain (ETC).

These carriers are sequentially arranged (Fig.11.7) and are responsible for the transfer of electrons from a given substrate to ultimately combine with a proton and oxygen to form water.

I. Nicotinamide nucleotides

Of the two coenzymes, NAD+ and NADP+, derived from the vitamin niacin, NAD+ is more actively involved in ETC.

NAD+ is reduced to NADH + H+ by dehydrogenases with the removal of two hydrogen atoms from the substrate (AH2).

The substrates include glyceraldehyde-3-phosphate, pyruvate, isocitrate, D-ketoglutarate, and malate.

NADPH + H+ produced by NADP+-dependent dehydrogenase is not usually a substrate for ETC.NADPH is more effectively utilized for anabolic reactions.

II. Flavoproteins

The enzyme NADH dehydrogenase (NADH: coenzyme Q reductase) is a flavoprotein with FMN as its prosthetic group.

The coenzyme FMN accepts two electrons and a proton to form FMNH2. NADH dehydrogenase is a complex enzyme closely associated with non-heme iron proteins (NHI) or iron-sulfur proteins (FeS).

Succinate drogenase (succinate-coenzyme Q reductase) is an enzyme found in the inner mitochondrial membrane.

It is also a flavoprotein with FAD as the coenzyme. This can accept two hydrogen atoms ($2H^+ + 2e^–$) from succinate.

III. Iron-sulfur proteins and Coenzyme Q :

The iron-sulfur (FeS) proteins exist in the oxidized (Fe^{3+}) or reduced (Fe^{2+}) state.

About half a dozen FeS proteins connected with the respiratory chain have been

identified.

However, the mechanism of action of iron-sulfur proteins in the ETC is not clearly understood.

One FeS participates in the transfer of electrons from FMN to coenzyme Q.

Other FeS proteins associated with cytochrome b and cytochrome c1 participate in the transport of electrons.

Coenzyme Q is also known as ubiquinone since it is ubiquitous in living systems.

It is a quinone derivative with a variable isoprenoid side chain.

The mammalian tissues possess a quinone with 10 isoprenoid units, which is known as coenzyme Q10 (CoQ10)

Coenzyme Q is a lipophilic electron carrier. It can accept electrons from $FMNH_2$ produced in the ETC by NADH dehydrogenase or $FADH_2$ produced outside the ETC (e.g., succinate dehydrogenase, acyl-CoA dehydrogenase).

Coenzyme Q is not found in mycobacteria. Vitamin K performs a similar function to coenzyme Q in these organisms.

Coenzyme Q has no known vitamin precursor in animals. It is directly synthesized in the body. (Refer to cholesterol biosynthesis.

IV. Cytochromes:

The cytochromes are conjugated proteins containing a heme group. The latter consists of a porphyrin ring with an iron atom.

The heme group of cytochromes differs from that found in the structure of hemoglobin and myoglobin.

The iron of heme in cytochromes is alternately oxidized (Fe^{3+}) and reduced (Fe^{2+}), which is essential for the transport of electrons in ETC.

This is in contrast to the heme iron of hemoglobin and myoglobin, which remains in the ferrous (Fe^{2+}) state.

Three cytochromes were initially discovered in the mammalian mitochondria.

They were designated as cytochrome a, b, and c depending on the type of heme present and the respective absorption spectrum.

Additional cytochromes, such as c1, b1, b2, and a3, were discovered later.

The electrons are transported from coenzyme Q to cytochromes (in the order) b, c1, c, a and a3.

The property of reversible oxidation reduction of heme iron Fe^{2+} Fe^{3+} present in cytochromes allows them to function as effective carriers of electrons in ETC.

Cytochrome c (mol. wt. 13,000) is a small protein containing 104 amino acids and a heme group. It is a central member of ETC with an intermediate redox potential.

It is rather loosely bound to inner mitochondrial membrane and can be easily extracted.

Cytochrome a and a3:

The term cytochrome oxidase is frequently used to collectively represent cytochrome a and a3 which is the terminal component of ETC.

Cytochrome oxidase is the only electron carrier, the heme iron of which can directly react with molecular oxygen.

Besides heme (with iron), this oxidase also contains copper that undergoes oxidation-reduction (Cu^{2+} Cu^{+}) during the transport of electrons.

In the final stage of ETC, the transported electrons, the free protons and the molecular oxygen combine to produce water.