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Bio chemistry

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Sheet ○ Slides

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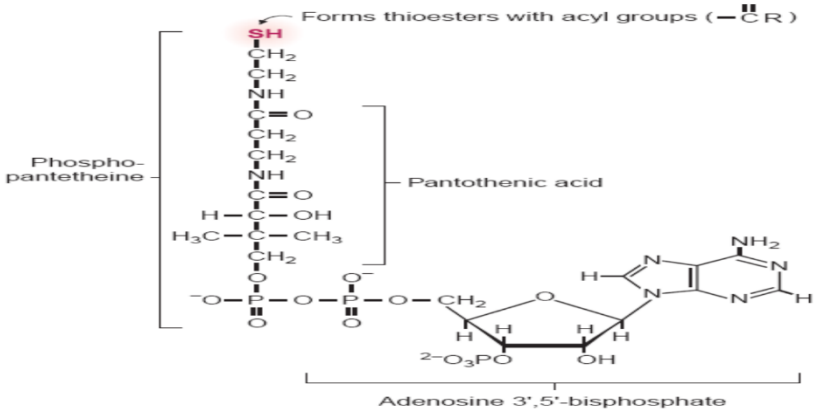
As we learned before, all chemical compounds that contain a phosphate group in their structure can donate it to give high amounts of energy. Moreover, Sulphur-carbon (S-C) bond gives high amounts of energy when broken, that bond is found in acetyl coA (S-C bond is a part of modified cystine).

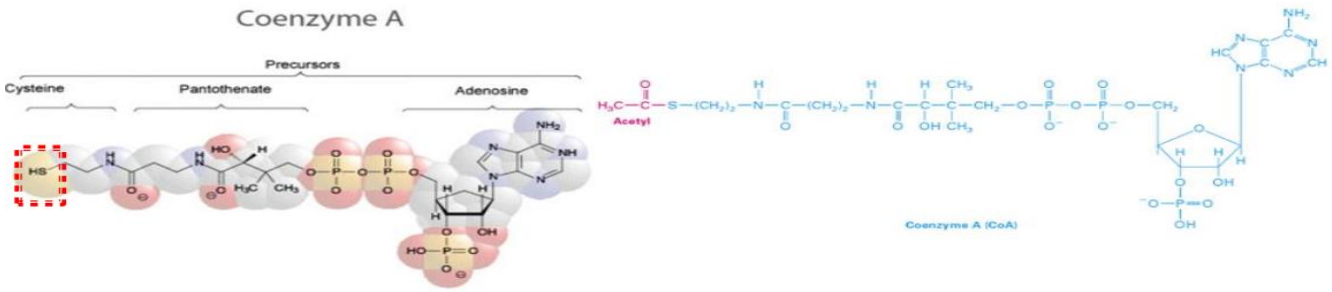
REMEMBER that CoA consists of adenosine, Pantothenic acid and cysteine. The bond between the functional group (sulfhydryl group) and the substrate has high amounts of energy so breaking it will release this energy.



All previous information are to emphasize that Acetyl-coA, the compound present at different food degradation pathways, can yield high amounts of energy when broken to Acetyl and coA . Thus, it can be used in coupling reactions.

For example, ACh , a neurotransmitter that causes muscle contraction, is synthesized from Acetate (2C molecule) + Choline (a nitrogenous base) .The reactant (acetate) as well as the energy needed for this reaction (S-C bond energy) come , at the same time , from Acetyl-coA. The same coupling concept applies for *phosphoryl transfer reactions where energy and the phosphate group itself come from ATP for example.*

- **Coenzyme A is a universal carrier (donor) of Acyl groups**
- **Forms a thio-ester bond with carboxyl group**



- $Acetyl\ CoA + H_2O \longrightarrow Acetate + CoA \quad \Delta G^\circ = -7.5kcal$
- $Acetylcholine + H_2O \longrightarrow Acetate + Choline\ \Delta G^\circ = -3\ kcal$

Now let us talk about thermogenesis (heat production). Thermogenesis is defined as the regulated process in which the body produces its energy that is expended for generating heat in addition to that expended for ATP production. This means that, through production of ATP, a specific amount of energy is released as heat, maintaining body temperature at **37o**. The two types of thermogenesis are shivering and non-shivering thermogenesis.

Shivering thermogenesis (ATP utilization): when you are exposed to a sudden cold, your body responds by asynchronous muscle contractions (shivering) in an uncontrolled way. By doing this, ATP is consumed to tell the body that more ATP is needed so it starts synthesizing it and as a by-product, heat is produced and the body temperature is back to normal.

Non-shivering thermogenesis (ATP production efficiency).

What do we mean by ATP production efficiency? Nutrients are the main source of energy. Imagine that you and your friend ate the same amount of food (same energy income) to maintain **37oC** (same outcome) then, would the amount of energy converted to heat (to maintain 37°**)** be the same in both of your bodies? Of course not, this energy depends on many factors such as: Gender, height, weight, place of living, surrounding environment, presence of diseases and administering drugs, etc.

Therefore, the body adapts how much energy lost to maintain temperature (producing heat) which is called **Adaptive Thermogenesis**.

Oxidation reduction reactions:

We divided enzymes into 6 categories. The one we are concerned with is oxidoreductases that catalyze Oxidation-reduction (Redox) reactions. Look at this oxidation reaction:

Fe^{2+}  Fe^{3+}

We noticed that ferrous ion Fe^{2+} was oxidized (lost one electron) to ferric ion (Fe^{3+}).

if we considered the bonds to which ferrous or ferric ions bind, then each ion binds to 4 N atoms in heme group. No change in bonds energy since the change is in the number of electrons only.

Although there is no change in bonds energy or in the structure but it is still considered a reaction and even catalyzed by an enzyme. That's what we mean by a redox reaction.

What about delta G, feasibility, stability and energy difference? We cannot use delta G alone with its previous studied concept (bond energy) to study these reactions. Actually, there is also another measure that we will talk about later. But for now, you must know delta G is not only concerned with bond energy.

Now let us talk about the relationship between electricity and redox reactions. Think of the process of charging your mobile phone. When you insert the charger into the power socket then electrons move from power plant to the electricity column then to your charger so that your phone charges. Have you ever thought about the reason electrons move in this direction (from the power plant to your phone)? The answer is electrical voltage difference when electrons move from high voltage(energy) to low voltage(energy).

On the contrary, solar panels generates high voltage to provide power plant with energy which means they change the direction of movement of electrons depending on potential gradient (from higher (solar panels) to lower (power plant)).

The potential difference principle applies to redox reaction since we have:

(1) a center which is a donor for electrons (high energy)

(2) a center which is an acceptor of electrons (low energy)

Keep in mind that each center can accept/lose electrons depending on the presence of other electron centers that precede or follow it.

This concept leads to redox potential (***E***) which is defined as POTENTIAL ENERGY that measures the tendency of oxidant/reductant to gain/lose electrons (to become reduced/oxidized).

Note:

- Reduction potential means the tendency of an oxidant (oxidizing agent) to gain electrons. (and the opposite for oxidation potential)
- For any redox couple (A, A-) at the same environment (to which protein bound), reduction potential and oxidation potential has the same value but different signs.
- Reduction potential is used more often.

Redox potential is concerned with electron centers (compound, atom, ion, molecule, etc.). Also, it is different from electronegativity that measures the ability of an atom to attract bond electrons toward itself.

Does redox potential have fixed or continuously changeable value? This depends on the electron center itself. For example, electron centers, that are always found in a certain state, have fixed redox potential like oxygen and those free molecules found in solutions. In contrast, those which bind to different molecules as well as those found in multiple environments have variable redox potential values such as heme group (its redox potential depends on to which protein it is bound). Heme group binds to different proteins such as: cytochrome oxidase, complex iii, myoglobin and hemoglobin in a different manner which alters its ability to lose/gain electrons and thus it has changeable redox potential value.

oxidation is associated with breaking down complex structures into more simple structures and thus losing electrons. While reduction is associated with building bonds. Like trapping electrons from Krebs cycle and packing them on electron carriers that enter electron transport chain (ETC).

ETC consists of 4 complexes numbered from 1-4 through which electrons keep moving. Electrons jump between these complexes without stopping. This is because there is a driving force and potential difference (redox potential) between every two electron centers.

Note:

- Oxidation and reduction must occur simultaneously
- Higher reduction potential means higher tendency to accept electrons, so electron moves from a lower reduction potential to a higher one.

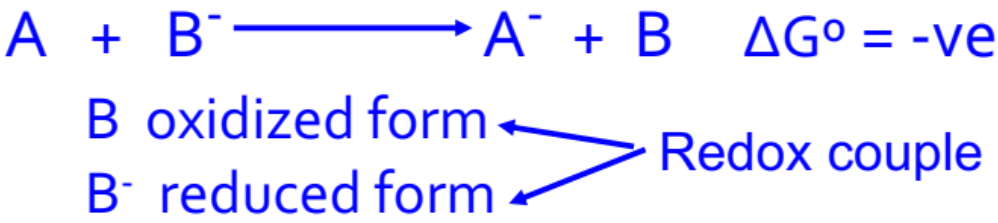
➢ **Oxidation:**

- ✓ Gain of Oxygen
- ✓ Loss of Hydrogen
- ✓ Loss of electrons

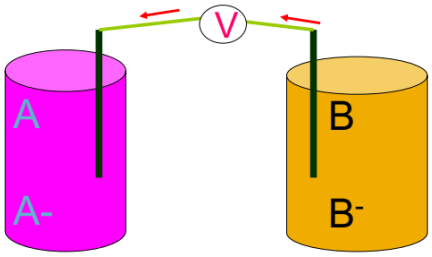
➢ ***Reduction:***

- ✓ Gain of Hydrogen
- ✓ Gain of electron
- ✓ Loss of Oxygen

Now look at this redox couple: (A) accepts electrons and is converted to the reduced form A- so we have a redox couple (A, A^-). Another redox couple is shown in this illustration.



Now, can we measure redox potential experimentally? The answer is **yes**. Scientists were able to measure reduction potential for a wide variety of materials with respect to hydrogen electrode (as a standard electrode ***E*° =0**) and they arranged these values from the more negative to the more positive value in a large scale. The more negative value has high capacity to lose electrons while the more positive value has high tendency to gain electrons. For example, if we have 2 reduction potentials: the first equals -600mv while the second equals -500mv then electrons move from the first to the second material.



The importance of this standard electrode is to obtain the exact value of reduction potential because if we used 2 materials of unknown reduction potential, then we will not be able to find the exact value for both since they are different. Another advantage of using hydrogen is that most materials can gain/lose hydrogen.

Reduction potential: Ability to accept electrons

Oxidized + e^-	➔ Reduced	*ΔE° (V)*
Succinate	α ketoglutarate	- 0.67
Acetate	Acetaldehyde	- 0.60
NAD^+	**NADH**	**- 0.32**
Acetaldehyde	Ethanol	- 0.20
Pyruvate	Lactate	- 0.19
Fumarate	Succinate	+ 0.03
$Cytochrome^{+3}$	$Cytochrome^{+2}$	+ 0.22
oxygen	**water**	**+ 0.82**

From the table, we notice 2 important points. Firstly, oxygen is the final electron acceptor for electrons (electrons from different nutritional materials are trapped by oxygen) thus it has the most positive reduction potential.

Secondly, NADH has a reduction potential (*E*°) of -320 mv thus it gives electrons to oxygen with *E*° =+820mv. This direction of electron movements fits the science since we already know that electron carriers like NADH after produced from Krebs cycle donate their electrons for materials with higher *E*.

As we talked before about ΔG and its relation to bond energy, we can say the difference in energy caused by reduction potential is another diameter of what ΔG measures. So, ΔG is not only concerned with bond energy. The reduction potential, not bond energy, is the driving force for electrons movement. Therefore, if we inverted the sign of reduction potential value then electrons will move in the backward direction. There must be a mathematic relation that governs the direction of electrons movement. Moreover, it should not contain any variable other than ΔG and ΔE.

$$\Delta G^o = - n f \Delta E^o$$

- F = Farady constant = 23.06 kcal/*Volt*

(n) constant: the number of electrons moving

Also, the following relation can be used:

$$\Delta G = - n f \Delta E$$

For a reaction to be favorable, spontaneous and exergonic (-ve ΔG) then ΔE must have a +ve value. The following example supports the previous statement.

NADH has a reduction potential $E°$= -320 mv thus it gives electrons to oxygen with $E°$=+820mv.

$\Delta E°$ = $E°$ (final oxygen) – $E°$ (initial NADH) = +820 – (- 320) = +1140 mv (positive value and spontaneous reaction)

As we seen before, the sign of ΔE° is +ve thus when scientists wrote equation, they inserted the -ve sign to fit the real situation.

Question:

Calculate ΔG^o of the following reaction

$$NADH + 1/2O_2 \longrightarrow NAD^+ + H_2O$$

$$NADH \longrightarrow NAD+ + 2e^- \quad \Delta E^o = +0.32\ V$$
$$O + 2e^- \longrightarrow O^{2-} \quad \Delta E^o = +0.82\ V$$

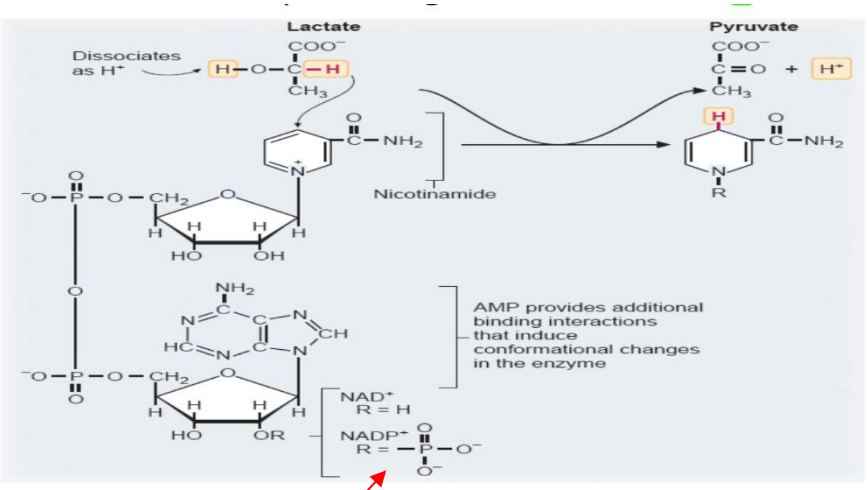
Solution:

$\Delta E°$ =1140 mv = 1.14 volt

$\Delta G° = -nf\ \Delta E°$ = -(2) (23.06)(1.14) ➔ ΔG^o = - 52.6 kcal/mol

Now, let us talk about electron carriers (that transports electrons to ETC). There are 2 main electron carriers: **NAD+** (niacin, B3) & **FAD** (riboflavin, B2).

- **NAD+** accepts a single hydride ion H^- (2 electrons) on nicotinic ring with one step, so it does not form a radical (will not be harmful) and thus can be found free as both NAD+/NADH in mitochondria/cytosol. As a result, it has a fixed reduction potential.

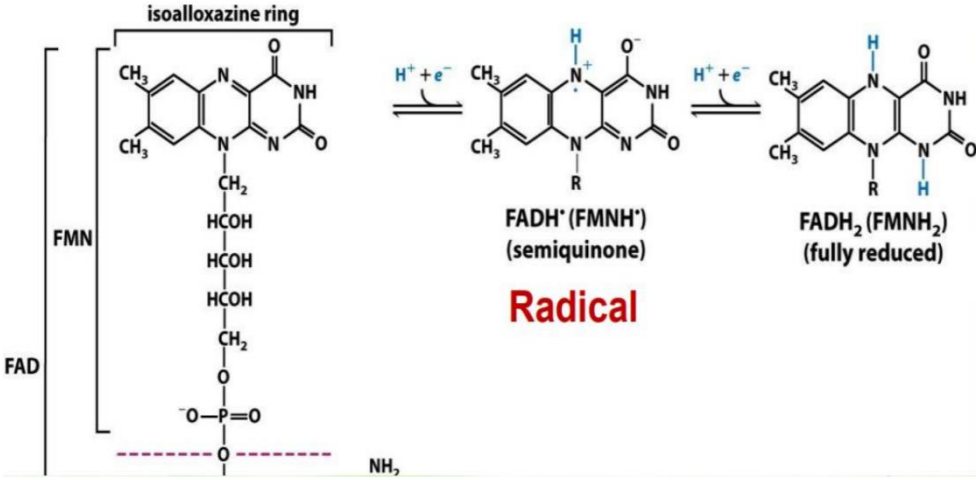


NADP+ is different from NAD+ only by a phosphate group instead of a hydrogen atom as shown in the previous figure.

Both of them carries 2 electrons but NAD+ participates in catabolism while NADP+ participates in anabolism. So, different structures that do the same function for better organization and regulation.

- **FAD** accepts 2 protons (2 electrons) sequentially since there are 2 H atoms thus it forms a radical intermediate and passes through (one electron/free radical state) that is harmful. Therefore, it cannot be found free in the cytosol and is always bound to proteins. Also, its reduction potential depends on the protein it is bound to.

FMN also carries 2 electrons sequentially, but for better organization: one works in anabolic reactions while the other in catabolic reactions.



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