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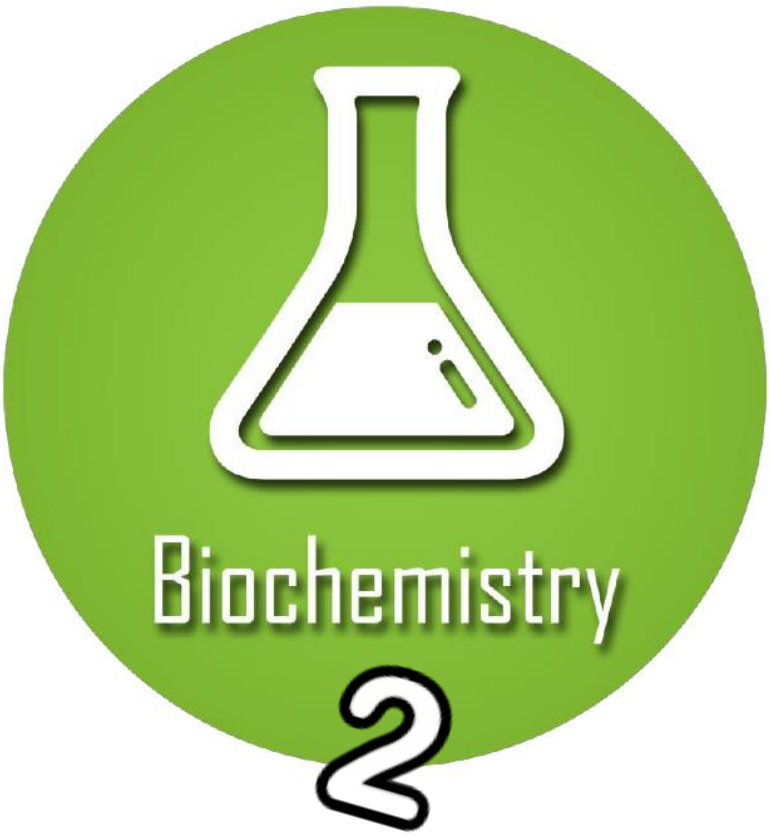
Medical Committee
The University Of Jordan




◉Sheet ○Slides

Number: 7

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Subject: Bioenergetics of the cell-2

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Q: When do we consider a molecule as a high energy molecule?

A: We consider a molecule as a high energy molecule when the degradation of this molecule gives you as much energy as that result in ATP hydrolysis or higher. (In another way: If its degradation gives you 7.3 kcal/mole or higher).

In the body there are a lot of endergonic reactions, which won't proceed spontaneously, it need energy to proceed. **From where we can provide this energy?(or: Body concepts in running endergonic reactions).**

**The first concept** the body deal with is the concept of **coupling**. In this concept we run endergonic reactions by the use of exergonic reactions.

Most commonly the exergonic reactions are**ATP hydrolysis**, and it fits for reactions that need phosphate, so use the phosphate from ATP and the energy which results in its hydrolysis.

Example: In the glycogen synthesis process (**Figure 1**), after glucose has entered, the cell it should be phosphorylated, this reaction is endergonic (it requires 3.3 kcal/mole). This reaction gets the Phosphate from ATP, so ATP will be hydrolysed and it will give 7.3 kcal/mole, so in total sum of energy, this step will end up with excess 4 kcal/mole.

**Note:** Here, the body considers the whole pathway as an energy unit. So in the previous example, when the reaction ended with excess energy, the body will use it to run subsequent reactions or to run previous reactions, and that's because the body considers the whole metabolic pathway as one unit and the pathway will be considered endergonic or exergonic depending on the energy levels of the first and the final materials. This is the same concept as in ΔG, ΔG doesn't care about intermediates produced during the reaction, it cares only about initial and final states and accordingly you consider if the reaction is spontaneous or not.

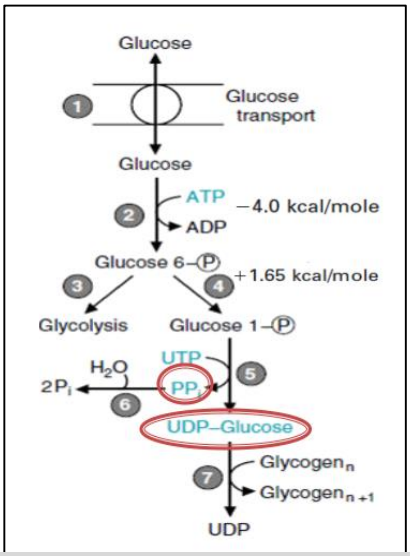


**Figure 1: Glycogen synthesis**

**The second concept is the use of high energy molecules:** We talked about ATP, but there are other molecules, such as UTP, GTP, CTP and TTP (All the nitrogen bases can be in three forms, monophosphate, diphosphate or triphosphate). ATP is the common molecule in energy degradation processes (Mostly, catabolic processes will end up by ATP).

While in anabolism (the building up of molecules) there is no difference in using any of these molecules, because the energy levels of ATP, TTP, GTP, CTP and UTP are the same.

But mostly, for a better regulation of processes, the body allocates each one for these molecules for a certain processes. (Example: for protein synthesis the body tries to use GTP. For lipid synthesis the body tries to use CTP, and for carbohydrates synthesis it tries to use UTP. And ATP is the general energy molecule that will be used here and there).

**Q: Why do the energy levels of these molecules are the same?**

A: Because it depends on the bond energy that depends on the structure. And all these molecules has 3 phosphates bounded to each other so they have the same structure in the area of bond breaking (the bond between the terminal two phosphates).

See step 5 in figure 1. The UTP is hydrolyzed to UDP and phosphate, and the phosphate will attach to another phosphate resulting in pyrophosphate (which also can be broken down to produce energy). So, the energy resulted from the UTP hydrolysis and the pyrophosphate will be used to run the endergonic reactions present in the pathway.

**The third concept is the use of high energy intermediates:** The metabolic pathway tries to generate intermediates which has a high energy level, and braking down of this intermediates will release energy that can be used in endergonic reactions. Example: In step 7 in figure 1, glucose is bound to UDP, breaking down the glucose from the phosphate of UDP will result in energy that will be used to attach glucose to the glycogen.

**The last concept is removing the products from the reaction** to favor the reaction to move forward and flip the sign of ΔG from positive to negative sign.

Coenzyme A (CoA) is usually bounded to different molecules and it will give energy upon hydrolysis.

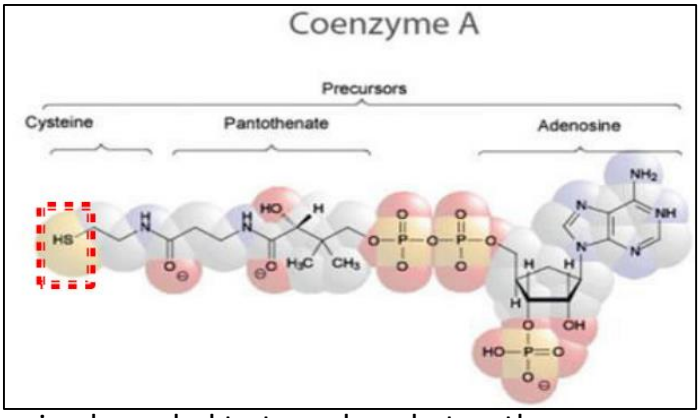


**Figure 2: Coenzyme A**

The structure of CoA (**Figure 2**): Adenosine bounded to two phosphates, then pantothenic acid (Vitamin B5) bounded to cysteine which has a free thiol

group. The sulphur in the thiol group is the place where the CoA binds to the carbon of any molecule.

**Note:** The energy value of carbon-sulphur bond (such as in Acetyl CoA) is comparable to ATP or even higher (it may reach 13 kcal/mole).

Example: Acetylcholine synthesis.

Acetate + Choline → Acetylcholine $\Delta G = +3$ kcal/mole (endergonic)

So how we provide energy to this reaction? We give it the acetate from an acetyl CoA hydrolysis.

Acetyl CoA + $H_2O$ → Acetate + CoA $\Delta G = -7.5$ kcal/mole (exergonic)

So acetyl CoA upon hydrolysis will donate the acetate to the choline, and the total energy level will become -4 kcal/mole.

**Note:** This is the same principle as ATP does through phosphoryl transfer reactions.

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# Thermogenesis

Thermogenesis is the process of making heat within the body.

Q: How the body preserve its temperature at 37°?

A: In krebs cycle, we will get electron carriers, this electron carriers go to the oxidative phosphorylation process and act on the electron transport chain. And in this chain you will transfer the electrons in a series of proteins. Upon electrons movement they will generate energy and this energy will pump the protons outside to generate ATP. However, this process is not 100% efficient, which means that there will be an energy loss, **and the lost energy will be used to generate heat.**And this is how the body keep its temperature at 37°.

**Q: Why did the body use this process to generate heat?**

A: Because it is going all the time, and the body preserve it temperature all the time. So this process suits this function.

There is two types of thermogenesis:

1. ***Shivering thermogenesis.***

**Q: Why does the body shiver involuntarily when the weather is cold?**

A: Because shivering is muscle contractions, and muscle contraction needs ATP, which tell the body to make more ATP, as by ATP synthesis you will generate heat.

### *2- Non-shivering thermogenesis. (The major type)*

It's also called adaptive thermogenesis. In this type there are variations between people. Such as people living in cold areas, their bodies will convert more energy to heat unlike people living in hot areas. Or people having some diseases. So the body adapts the amount of energy converted to heat according its situation.

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## Oxidation-Reduction (Redox) reactions:

Remember: The first class of enzymes is ***oxidoreductases.***

Theoretically, any reaction in the world is a dealing with electrons, by breaking bonds or forming new ones.

Essentially, there are reactions which involve movement of electrons from one place to another. These are the redox reactions, which are catalysed by the enzymes called ***oxidoreductases.***

**Q: In these reactions, what makes the electrons to move from one place to another**?

A: Because there is a voltage (فرق جهد) between the two places, the electrons will move from the high voltage area to the low voltage area to achieve higher stability.

**Q: Why there are voltage differences between different places?**

A: Because there are differences in the chemical structures of molecules. So the properties of different structures is not the same, and one of these properties is the willingness to donate electrons and the willingness to accept electrons.

The willingness to accept electrons is called **the reduction potential**.

***Reduction potential***: the ability to be reduced.

**Note:** This potential is a property of the material, regardless it actually accepted or donated electrons.

**Note:** It is similar to electronegativity, but electronegativity is at the level of atoms. But the reduction potential we are dealing with the whole proteins which contain many atoms.

***Example***: In Heme, there is iron, when it accept an electron the Heme becomes reduced. And if then the iron donates an electron the Heme will become oxidized and vice versa.

***Oxidation-reduction reactions*** always occur simultaneously. (The molecule which is oxidized will reduce another molecule).

**Remember:** ΔG considers the favorability of any reaction.

In redox reactions the voltage can tell the favorability of the reaction.

So, there must be a relationship between ΔG and the voltage.

And this equation shows the relationship.

$$\Delta G = -nf\Delta E$$

or: $\Delta G^o = -nf\Delta E^o$

ΔE: Reduction potential difference. ($\Delta E = E_{Acceptor} - E_{Donor}$)

n: number of electrons involved in the reaction (which moved from the oxidized molecule to the reduced molecule) .

f: Faraday's constant (23.1 Kcal/mol. V)

We notice that ΔE is related linearly to ΔG. And there is no other variables consider the favorability of the reaction.

**Remember:** $NAD^+$ accepts two electrons in the form of hydride ion ($H^-$).

**Note:** The more E(reduction potential) is positive, the more the ability to accept electrons, and the more E(reduction potential) is negative, the more the ability to donate electrons.

When we eat, the food will be degraded in the stomach and the intestines, then they will be absorbed and enter the cells as monomers. In the cells the nutrients (Carbohydrates, Proteins and lipids) will be further degraded and their bonds will be broken. Bonds breaking are oxidation reactions. The cells degrade nutrients until reaching acetyl CoA. Acetyl CoA then enters the krebs cycle and the bond between its two carbon atoms will break and the two carbon atoms exit the krebs cycle as $CO_2$, each carbon atom exit alone one by one. All these degradation processes is done to finally get energy. So the material oxidation (food degradation) results in ATP formation. Now, krebs cycle results in NADH and $FADH_2$, these electron carriers go to the electron transport chain and the electrons move from a protein to another until they reach $O_2$, and it react to hydrogen to become water.

We already know that the electrons move according to the voltage. So as the **$O_2$** is the final electron acceptor that means that **it has the most positive reduction potential.** It is the best material within the body that can accept these electrons.

E for $O_2$ by accepting electrons = 0.820 approximately.

When electrons move from NADH to finally reach $O_2$→ E = -0.320

When electrons move from $FADH_2$ to finally reach $O_2$→E = -0.200

**Note:** The negative charge indicates that these molecules donated electrons (have the willingness to donate).

As we have ΔE, we should have ΔG.

ΔG resulting from electrons donated by NADH = -53 kcal/mole

ΔG resulting from electrons donated by $FADH_2$ = -41 kcal/mole

We notice that the NADH pathway is more favorable than $FADH_2$ because the reduction potential of NADH is higher than $FADH_2$. ***(Note: we compare the numerical values regardless the sign, because the sign is just to tell if the molecule is a donor or an acceptor).***

## A quick look at NAD+ and FAD+:

NAD+ has a nicotinic ring. NAD+ accepts two electrons in the form of hydride ion ($H^-$), the two electrons are coming and once, and they are released from the molecule at once, it can't accept one electron alone. So it only NAD+ or NADH, it doesn't enter the free radical state. And this why that you can find free NAD+ or NADH in the cytoplasm, mitochondrial matrix or within the nucleus.

Accordingly, **the reduction potential of NAD+ or NADH is always constant (=-0.320).** Why? Because the reduction potential depends on the stricter, and the structure of NAD+ or NADH is always constant.

But FAD, accepts two electrons in the form of hydrogen atoms each one at a place and one by one ***(not at the same time).*** So it can enter the free radical state and becomes dangerous, so you can't find free FAD, it is always contained within a protein or an enzyme. **So the reduction potential in not constant** because it is contained in different structure. (According to the type of amino acids surrounding the FAD, the reduction potential will change).

**Q: How much is the reduction potential of FAD?**

A: You can't determine. Because the question did not specify the enzyme that contains the FAD.

# *(The lecture is over)*

# ***Test yourself !!***

1. The free energy change at standard conditions for the conversion of glucose 6- P to glucose 1-P is +1.65 Kcal/mol. What is the ratio of [ glucose 1-P] to [glucose 6-P] at equilibrium?

( Assume that RT = 0.593Kcal/mol)

a. 0.0593 c.0.62
b. 0.593 d.0.062

2. Given a free energy change at standard conditions of +1.65 Kcal/mol for the conversion of glucose 6-P to glucose 1-P and a

free energy change at standard conditions of -4.0 Kcal/mol for the conversion of glucose + ATP to glucose 6-P +ADP, what is the value of the free energy change at standard conditions for the conversion of glucose to glucose 1-P?

a. +2.35 Kcal/mol
b. -2.35 Kcal/mol
c. +5.65 Kcal/mol
d. – 5.65 Kcal/mol

3. Suppose that you have 4 materials A, B, C and D and they undergo the following reactions, dependant on them and their information , the correct arrangement of these materials according to increasing in reduction potential value E should be:

$A + B^{+2} \longrightarrow B + A^{+2}$(endergonic reaction)

$C + D^{+2} \longrightarrow D + C^{+2}$ ( difference in reduction potential is +0.89 V)

$C + B^{+2} \longrightarrow B + C^{+2}$ ( free energy change is -0.78 Kcal/mol)

$A + D^{+2} \longrightarrow D + A^{+2}$ ( spontaneous reaction)

a. D, A, B,C
b. C, B, A, D
c. D, B, C, A
d. C, A, B , D

4. The highest energy phosphate bond in ATP is located between which of the following groups:
   a. Adenosine and phosphate
   b. Ribose and phosphate
   c. Ribose and adenine
   d. Two phosphate groups

5. Which statement best describes the direction a chemical reaction will follow?
   a. A reaction with positive free energy will proceed in a forward direction if the substrate concentration is raised high enough.

b. Under standard conditions, a reaction will proceed in a forward direction if free energy is positive.
c. The direction of a reaction is independent of the initial substrate and product concentrations, because the direction is determined by the change in free energy.
d. The enzyme for the reaction must be working at higher than 50% of its maximum efficiency for the reaction to proceed in a forward direction.

***<u>The answers:</u>***

1. D
2. B
3. A
4. D
5. A

***(Now, the sheet is over)***

***Sorry for any mistake***
***Good luck*** ☺

# ***<u>The End</u>***