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Biochemistry

starchlipidproteinamine carbohydratesisomersketone

Doctor 2017 | Medicine | JU

◉ Sheet ○ Slides

Done By

Saba Alfayoumi

Contributed in the Scientific Correction

Shehab jaber

Contributed in the Grammatical Correction

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Doctor

Nafith Abu Tarboush

For the first energy lectures, you just need to know the meaning of Kreps cycle and oxidative phosphorylation as general topics that will help explain other topics.

Stages of energy production:

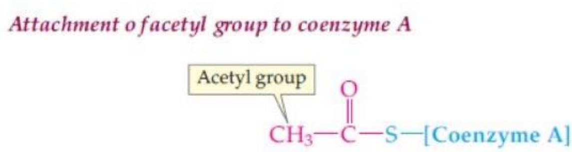
In order to produce energy, there are 4 stages (steps):

Stage 1.. Digestion: it includes ingestion of food, degradation, absorption then all molecules will be moved to the blood so it can reache all cells.

Food moves from Mouth > stomach > small intestine and during this movement:

- Carbohydrates will be degraded to glucose & other sugars.
- Proteins will be degraded to amino acids.
- Triacylglycerols will be degraded to glycerol plus fatty acids.

Stage 2.. (Acetyl-coenzyme A): Every molecule that results from the first stage will be broken down until it reaches a common molecule which is Acetyl CoA.

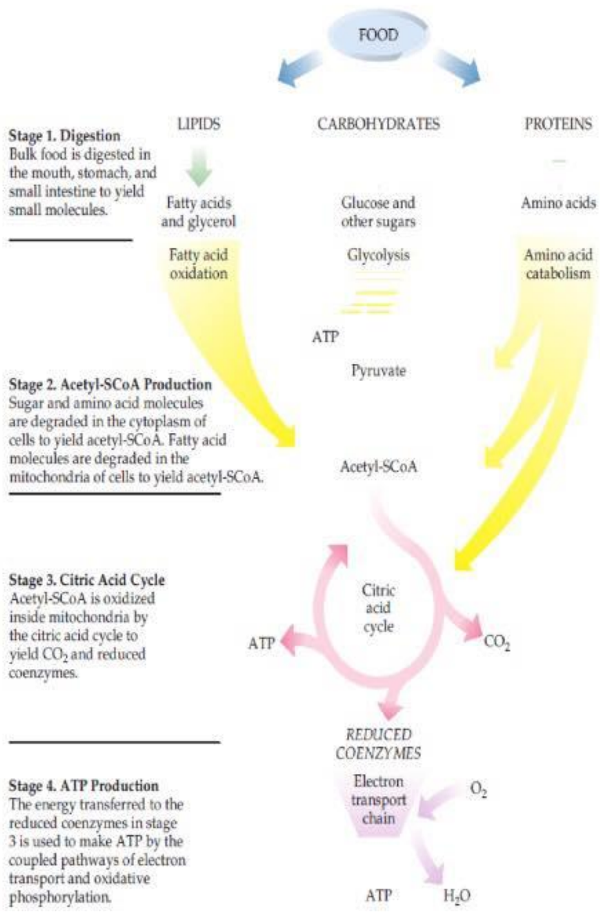


Stage 3.. citric acid cycle: Acetyl CoA enters the Kreps cycle seeking for energy production and it produces molecules that carry electrons(NADH and FADH2).

Stage 4.. electron transfer chain & oxidative phosphorylation:

Oxidative phosphorylation is the phosphorylation of ATP using oxidation-reduction reactions (transfer electrons from NADH and FADH2 to oxygen).

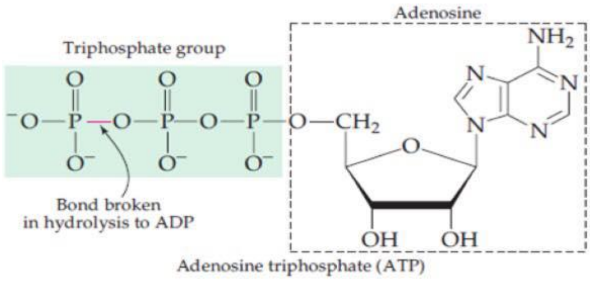
Molecules generated from Kreps cycle goes to the electron transport chain and are coupled with the procedure of ATP production (oxidative phosphorylation).



ATP:

It has a triphosphate group and breaking down each P—O bond gives energy because as we all know, breaking down bonds gives energy and building up bonds needs energy.

It's the main source of energy for most reactions so <u>it's the energy currency of the cell</u> and it determines the amount of energy the cell has.



There are many molecules that can produce energy, one of which is ATP which is the most common molecule used.

P-O & P-C bonds are high energy bonds so it gives energy when it's broken.

Why ATP between all these molecules that gives energy?

NOT because it has 3 phosphate or it has high energy or the negative charges it carries.

Rather it's because it has an intermediate energy value, so it can be coupled easily.

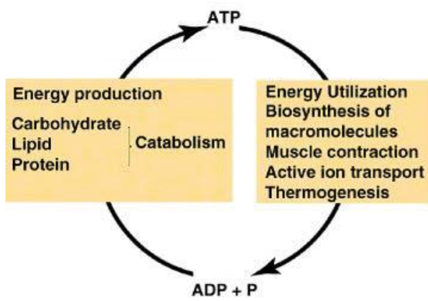
Compound +H_2O	Product + phosphate	$\Delta G°$
Phosphoenol pyruvate	Pyruvate	-14.8
1,3 bisphosphoglycerate	3 phosphoglycerate	-11.8
Creatine phosphate	Creatine	- 10.3
ATP	**ADP**	**- 7.3**
Glucose 1- phosphate	Glucose	-5.0
Glucose 6- phosphate	Glucose	-3.3

All these reactions are included in the Glycolytic pathway except Creatine phosphate > Creatine.

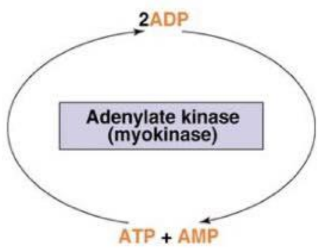
Note: any molecule containing phosphate will release energy when it loses the phosphate.

Just like money.. as the best currency used daily in Jordan is 5 or 10 JOD not 50 JOD because it's hard to change it, and it's also not small coins.

So.. we need a molecule with an intermediate amount of energy (ATP) so it can be broken down and resynthesized easily (the same amount of energy released from brakeage of ATP to ADP must be supplied to ADP to synthesis ATP again).



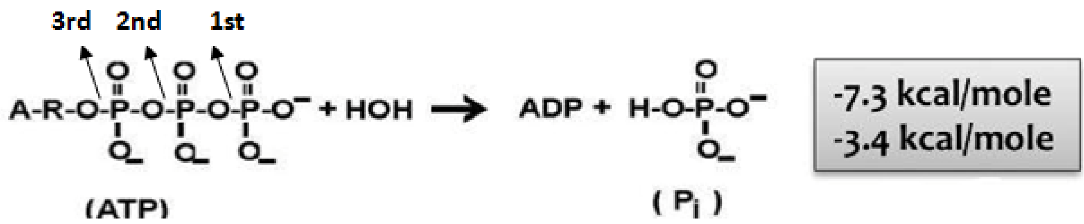
This means that if we assume that breaking P—O bond in ATP gives 20 kcal/mole, it means that I need a reaction in the body that gives 20 kcal/mole when it breaks in order to use this energy to form ATP again and this is not actually found



in the body. So we need a molecule with an intermediate energy value that suffices most reactions in the body by using 1molecule of ATP (when I need more I can use 2 or 3 ATPs).

There are also many reactions that give the same amount of energy that ATP produces so it can compensate ATP.

The amount of energy that ATP gives:



What determines the amount of energy a bond has is the atoms that are involved directly in the bond (phosphate and oxygen for example in ATP) and the distribution of atoms around this bond which makes strain on the bond so it changes the energy of the bond.

For example: **the first P—O bond** in the ATP gives 7.3 kcal/mole and if we look at **the second P—O bond** we find that it's identical regarding the atoms involved directly and the distribution of atoms around the bond, so if we break the second bond it will give the same amount of energy 7.3 kcal/mole. But **the third P—O bond** differs in the distribution of atoms around the bond so we must know that the energy it has will be different (we don't know if it's higher or lower or what's the exact energy value > here in this example it's given in the slides that the third bond contain 3.4 kcal/mole).

So it means that I can't say that the separation of the 3 phosphate molecules from ATP gives 21 kcal/mole because even if the atoms are the same (phosphate), bonds have different energy content due to different atom distribution.

Can ATP be stored in the body?why?

No, it can't be stored in the body because it has high molecular weight (551g/mole)

This table shows the amount of ATP needed by selective tissues at resting state, which is 90.6 moles/day so if there

Tissue	ATP turnover (mole/day)
Brain	20.4
Heart	11.4
Kidney	17.4
Liver	21.6
Muscle	19.8
Total	90.6

is an organ in our body can store ATP, it must store 50 kg for each day processes!!!!

*That's why all body cells function to produce ATP by oxidative phosphorylation in mitochondria (except RBCs which don't have mitochondria). ATP can be stored for short-term purposes to be used within 5 minutes. So as food in the cells is gradually oxidized, the released energy is used to re-form the ATP so that the cell always maintains a supply of this essential molecule.

Metabolism And Metabolic pathways:

Why do we need energy?

(1) the performance of mechanical work in muscle contraction and cellular movements.

(2) the active transport of molecules and ions

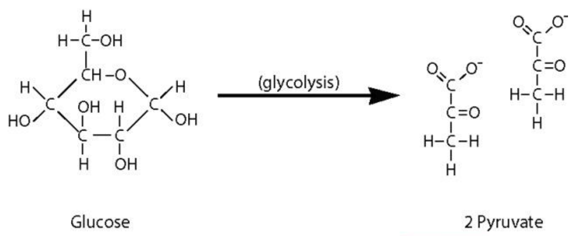
(3) the synthesis of macromolecules and other biomolecules from simple precursors.

Sun is the main source of energy, it gives energy to plants (autotrophs) to produce their own food and then animals (heterotrophs)will feed on plants, then human can eat both of them to get his food.

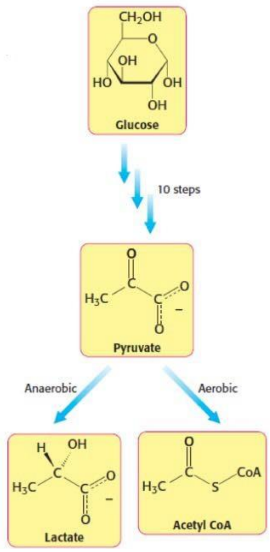
*Cellular metabolism: the sum of the total biochemical activities of all cells (anabolism and catabolism).

Mainly for energy generation

*Metabolism consists of energy-yielding (exergonic) and energy-requiring (endergonic) reactions.



Metabolic processes in our body occur in Pathways (multiple reactions happen to go from reactant to the desired product).NO single reactions occur alone. As simple as glycolysis, it's a simple reaction but to do this reaction in the body it needs 10 steps.



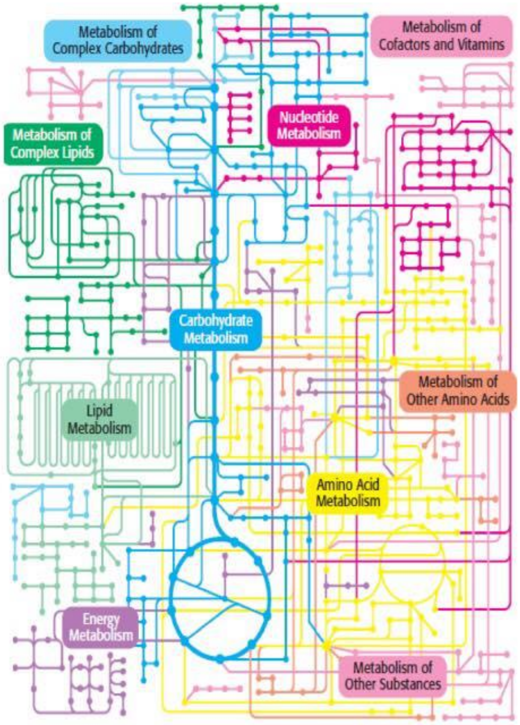
Pathways in the body are treated as single reactions with respect to thermodynamics and bioenergetics, So if I know the starting molecule and the end molecule, I can know if this pathway is exergonic or endergonic.

Usually, degradation pathways $\longrightarrow$ exergonic/ gives energy/ $-\Delta G$. e.g. glycogenolysis.

Building (anabolism) pathways $\longrightarrow$ endergonic/ needs energy/ $+\Delta G$. e.g. glycogen synthesis.

$$\text{glucose} + O_2 \longrightarrow CO_2 + H_2O$$

This reaction outside the body has a ΔG = -680 kcal/mole and when this reaction happens in the body it undergoes 21 steps pathway and it gives 680 kcal/mole so a pathway will give or take the same amount of energy as a single reaction regardless how many steps there are in the pathway.



Biochemical pathways in the body intersect each other. Why?

__To conserve energy__. If we assume that each pathway is separated from the other pathways, this means that each one will produce ATP by breaking down cellular molecules, that results in excess production of ATP that isn't needed so it will be lost. But by intersecting regulation can take place to control these processes leading to harmony between all pathways (ex: when carbohydrates are abundant in the cell it can for example inhibit lipid metabolism to stop the degradation of both carbohydrates and lipids at the same time so it conserves energy).

In other words, this intersecting balances metabolic supply and demand, averting deficits or surpluses of important cellular molecules.

What makes these pathways intersect with each other?

__Allosteric enzymes__. Because they have catalytic and regulatory subunits, and on the regulatory subunits there are many sites where molecules can bind.

For example, the key enzyme of glycolysis: the molecules that bind to the regulatory subunits determine the efficiency of this enzyme (either it will work 90% or 50% or completely inhibited).

*These pathways are:

- Interdependent on each other.

- Subjected to thermodynamics laws.

-Their activity is coordinated by sensitive means of communication.

- Allosteric enzymes are the predominant regulators.

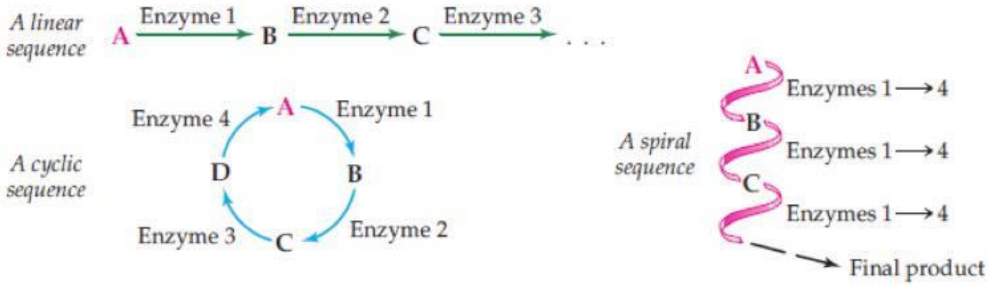
- Biosynthetic & degradative pathways are almost always distinct (regulation).

- Metabolic pathways are linear, cyclic or spiral:

Linear pathway: each step leads to the other one till we finally reach the final step and each step is catalyzed by different enzyme. E.g. glycolysis (10 steps linear pathway).

Cyclic pathway: The same as the linear pathway but it differs in the last step which generates the first molecule the cycle started with. E.g. Kreps cycle, Urea cycle.

Spiral pathway: we aren't going to now all the details regarding this type but what mostly makes it special is that every step is catalyzed by the same enzymes.



Any pathway in the body is either exergonic or endergonic. Exergonic reactions are easy to understand because the reactants have higher energy than the products and everything in the world seeks to stability so it's spontaneous (spontaneous doesn't mean it happens alone by itself, actually it needs to break the activation energy barrier so it needs enzymes that decrease the activation energy).

You have to differentiate between exergonic and endergonic reactions and to know the concept behind each reaction?

All reactions that goes from complex structures to simple structures are exergonic and all reactions that goes simple to more complex structures are endergonic.

Complex structures ➔ simple structures

Proteins $\longrightarrow$ amino acids

Starch $\longrightarrow$ n glucose

glucose + O_2 $\longrightarrow$ $CO_2 + H_2O$

More specifically

- **Hydrolysis reactions:** All hydrolases use water to break down bonds so it catalyzes exergonic reactions. Such as proteases which breaks down proteins and amino acids.

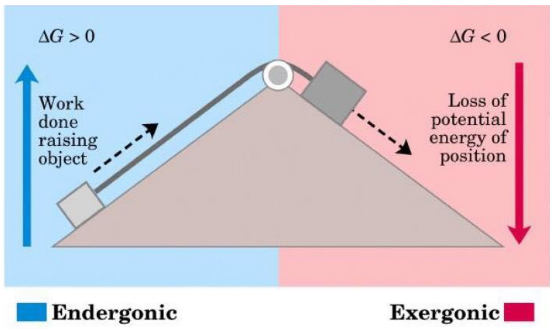
- **Decarboxylation reactions (release of CO2) (exergonic)**: pyruvate (C3) → acetyl-CoA(C2) +CO2

- **Oxidation withO2 (exergonic)**

Endergonic reactions need energy, **so how does the body make it possible for an endergonic reaction to happen?**

1.Changing the concentrations of reactants and products (making the concentration of reactant much higher than the concentration of products so the forward reaction will be favorable).

2.Coupling of reactions:



That's by getting the material needed in the reaction from another material that gives energy when it's broken, so the other material gives us both the material and the energy needed for the reaction.

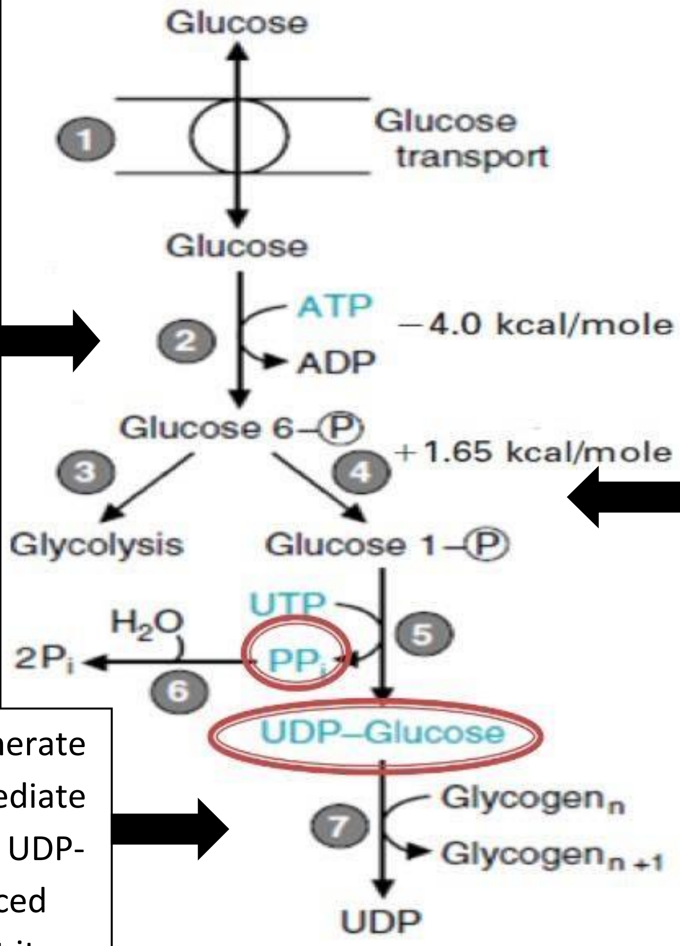
E.g. Phosphoryl transfer reactions need phosphate and energy and that can be got from ATP which gives us both phosphate and the energy needed.

It's not just ATP that can be used, we can also use any other molecule that gives energy and part of this molecule is needed in my reaction.

Synthesis of glycogen:

It's an anabolic pathway (building up pathway).

Step 2 needs 3.3 kcal/mole and a phosphate and we can get that from ATP that gives 7.3 kcal/mole and phosphate so here we will have some excess energy 4 kcal/mole (this excess energy can be used during the pathway or in other reactions).



Some pathways generate high energy intermediate like in step 5 where UDP-Glucose is produced which means that its separation will supply the energy needed for the pathway. So here in step 7, separation of UDP from glucose gives the energy to attach the glucose to glycogen.

Step 4 gets its energy by playing with the concentrations. As ΔG Depends on Substrate and Product Concentration. The original (products/reactants) ratio is 6/94 so ΔG= +1.65 kcal/mol but if we can withdraw some of the products out then the ratio will become 3/94 and ΔG= -0.4kcal/mol so the reaction will become exergonic.

How do our cells get energy for unfavorable biochemical work?

I. ΔG0 Values are additive

i. Through phosphoryl transfer reactions

- Step 2 (+3.3 vs. -4 kcal/mole).

- Step 2 + 4 = -2.35 kcal/mole.

*The net value for synthesis is irrelevant to the presence or absence of enzymes.

ii. Activated intermediates (step 4 is facilitated by steps 5&6).

II. ΔG Depends on Substrate and Product Concentration just like step 4.

ADP/ GDP/ UDP/ CDP/ TDP + molecule = high energy intermediate

To produce high energy intermediates we need high energy molecules such as ATP, GTP, UTP, CTP (they all have the same amount of energy in the first 2 P--O bonds = 7.3 kcal/mole).

Why there are many forms of these high energy molecules?

For better regulation in the body.

For energy purposes: the most commonly used molecule is **ATP**.

For protein metabolism: the most commonly used molecule is **GTP**.

For lipid metabolism: the most commonly used molecule is **CTP**.

For carbohydrate metabolism: the most commonly used molecule is **UTP**.

GOOD LUCK ☺