Pentose cycle, metabolism of fructose, galactose and glucuronic acid

Content of subsection:

Pentose cycle (hexose monophosphate shunt)

Pentose Cycle

Pentose Cycle Diagram The pentose cycle allows the **direct oxidation of glucose** to CO_2 without involving the Krebs cycle and respiratory chain.

Coenzyme $NADP^+$ molecules are used as a cofactor for dehydrogenases in the pentose cycle, which after receiving reduction equivalents (H atoms) are reduced to NADPH + H^+. These can be used in many places in the cell - they serve as sources of reducing equivalents during biosynthesis (e.g. synthesis of fatty acids or steroid substances), they help antioxidant protection of cells (including the system glutathione) or participate in the metabolism of foreign substances.

In the pentose cycle, ``ribose-5-P *(precursor in the synthesis of nucleic acids) or many other monosaccharides can also be formed.*
The purpose of the pentose cycle is not direct energy gain, since NADPH cannot be oxidized in the respiratory chain, but rather:

1) **NADPH gain** - the pentose cycle is the main producer of NADPH in the cell;

2) **ribose-5-P gain**;

3) **mutual transformations of monosaccharides**, used for example in the synthesis of glycoproteins.

The pentose cycle is localized in the cytosol (especially of liver cells, adipose tissue, testicles, adrenal cortex, then in erythrocytes or in the lactating mammary gland, but enzymes are found in all tissues).

Within the pentose cycle, we can distinguish two basic phases - "oxidative" and "non-oxidative" (regenerative).

Oxidative (oxidative) phase

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In addition to AcCoA, **propionyl-CoA** is also formed by oxidation of odd-chain fatty acids. This is first **carboxylated to methylmalonyl-CoA'**, which is converted to **succinyl-CoA** - an intermediate of the **Krebs cycle'**. Through conversion to oxaloacetate, it can participate in **gluconeogenesis** - glucose can be synthesized from these fatty acids. However, very few fatty acids with an odd number of carbon atoms are found in the body.

The **pentose cycle** is a catabolic event that provides reduced cofactors NADPH and five-carbon saccharides, or pentoses. It is a metabolic conversion of glucose, the goal of which is not the creation of ATP.

Course of the oxidative phase of the pentose cycle

During the *oxidative phase* of the pentose cycle, the glucose-6-P molecule is oxidized to the ribulose-5-P molecule. At the same time, CO_2 is released and two NADPH + H^+ molecules are obtained.

File:Oxidation.jpg

Scheme of the oxidative phase of the pentose cycle

Its course is summarized by the following equations:

'*Glucose-6-phosphate + 2 $NADP^+$ → CO_2 + 2 NADPH+H^+ + ribulose-5-phosphate*'

Of the reactions of the first phase, the initial reaction catalyzed by ``glucose-6-phosphate dehydrogenase *is important. This* ***irreversible*** **reaction is the main regulatory step of the pentose cycle.**

The rate of the oxidative phase of the pentose cycle

The **speed** of the entire metabolic pathway depends on the activity of two dehydrogenation reactions, which depend on the availability of $NADP^+$ (i.e. the oxidized form of the coenzyme). With a lack of $NADP^+$, the rate of the pentose cycle decreases, in other words: an excess of NADPH "slows down" the oxidative phase of the pentose cycle.

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Links

Related Articles

- Pentose cycle
- NADPH

External links

- Pentose cycle (Czech Wikipedia) (https://cs.wikipedia.org/wiki/Pent%C3%B3zofosf%C3%A1tov%C3%BD_cyklus%7C)

Regenerative (non-oxidative) phase

The **pentose cycle** is a catabolic process that provides reduced cofactors NADPH and five-carbon carbohydrates, or pentoses. It is a metabolic conversion of glucose, which goal is not to create ATP.

Progress of the regeneration phase of the pentose cycle

In the regeneration phase, mutual transformations of phosphorylated monosaccharide molecules occur.

These reactions are **freely reversible** (reversible).

Basic Scheme

The basic diagram of the regeneration phase of the pentose cycle could be simply written as:

3 C5 → 2 C6 + C3

3 Ribulose-5-P → 2 fructose-6-P + glyceraldehyde-3-P

More detailed diagram

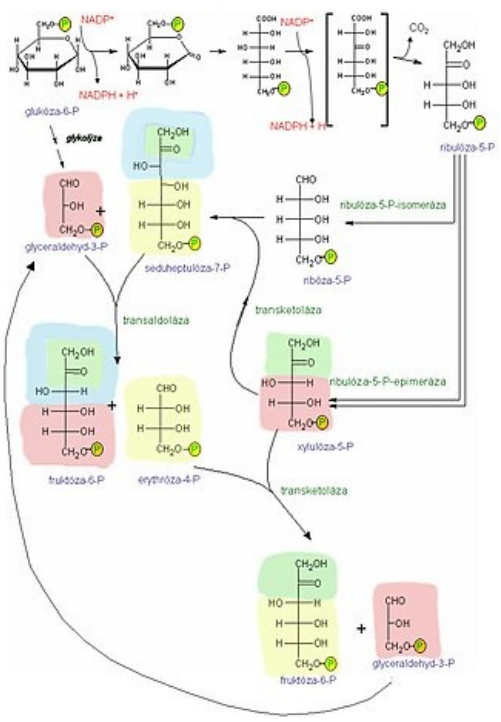
At a closer look:

1) Conversion of *ribulose-5-P* to *ribose-5-P* (ketosis is changed to aldose with the help of isomerase) or to *xylulose-5-P* (catalyzed by epimerase)

2) The following is a pair of reactions expressed by equations:

C5 + C5 ↔ C3 + C7 ↔ C6 + C4

Xylulose-5-P + ribose-5-P ↔ glyceraldehyde-3-P + sedoheptulose-7-P ↔ Fru-6-P + erythrose-4 -P



Pentose cycle

These reactions are catalyzed by two transferases – *transketolase* and *transaldolase*.

Transketolase transports two-carbon units from *xylulose-5-P* (ketose) to *ribose-5-P* to form *glyceraldehyde-3-P* and *sedoheptulose-7-P* (the cofactor of the enzyme is a derivative of vitamin B1 – *thiamine diphosphate*).

Transaldolase transfers three-carbon units from *sedoheptulose-7-P* (ketosis) to the aldehyde group of *glyceraldehyde-3-P*.

In general, carbon grafts (C3- and C2-units) are made from ketoses and aldoses become their recipient.

The result is that a shorter aldose is formed from ketose and a longer ketose is formed from aldose.

3) In order not to accumulate unnecessary *erythrose-4-P*, its reaction with *xylulose-5-P* follows:

C4 + C5 → C3 + C6

Erythrose-4-P + Xylulose-5-P → Glyceraldehyde-3-P + Fructose-6-P

The resulting products of the second phase, *fructose-6-P* and *glyceraldehyde-3-P*, can be either burned by the reactions of glycolysis and gluconeogenesis (also take place in the cytoplasm), or converted to *glucose-6-P*. This can again enter the oxidative phase of the cycle, and the pentose cycle is closed. At this point we can clearly see how glycolysis/gluconeogenesis is closely linked to the pentose cycle.

Sometimes we can even come across the claim that the pentose cycle is their divagation.

If we look at the pentose cycle as an **alternative pathway of glucose oxidation**, we can write the summary equation:

6 Glucose-6-P → 6 CO_2 + 6 ribulose-5-P + 12 NADPH+ H^+

6 Ribulose-5-P →→→ regeneration phase and gluconeogenesis →→→ 5 glucose-6-P

This occurs if the cell needs to **maximize NADPH gain**.

However, the pentose cycle can also serve as a source of *ribose-5-P* or other monosaccharides. If the cell needs them (and does not require NADPH), the second phase of the cycle can be reversed, and by the opposite sequence of reactions, *glyceraldehyde-3-P* and *fructose-6-P* are pumped out of glycolysis, and it gradually changes to *ribose-5-P* or other monosaccharides.

Regulation of the pentose cycle

As already stated above, the pentose cycle is regulated at the level of availability of the coenzyme $NADP^+$. If the result reduced form of NADPH is not pumped out and reoxidized in other metabolic processes, reactions that require the oxidized form of this coenzyme are inhibited. The reduction of $NADP^+$ to NADPH is catalyzed by *glucose-6-phosphate dehydrogenase* and *6-phosphogluconate dehydrogenase*. The synthesis of key enzymes is also induced by insulin. Prolactin does the same during lactation.

Clinical correlation:

Glucose-6-phosphate dehydrogenase deficiency is considered the most widespread enzymatic defect worldwide - the number of affected is estimated at 400 million people (mainly in Africa, the Mediterranean, the Middle East and Asia). One of its consequences is the development of **hemolytic anemia** (due to disruption of the antioxidant systems of erythrocytes). You can find more detailed information in the multimedia scripts Functions of cells and the human body, 3. LF UK. (http://fblt.cz/skripta/v-krev-a-organy-imunitniho-systemu/4-hemostaza/)

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Fontana J., Trnka J., Maďa P., Ivák P. et al.: Transformation of substances and energy in the cell. In: Functions of cells and the human body : Multimedia scripts.

Category: Biochemistry Category: FBLT

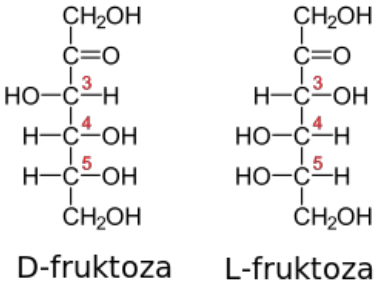
Metabolism of fructose

Metabolism of fructose

We can take fructose in food either free (fruit, honey) or in the form of sucrose disaccharide.

It is broken down by sucrose into fructose and glucose. Fructose is absorbed into enterocytes by facilitated diffusion through a specific transporter. A smaller part of fructose is already converted into glucose in the enterocytes (via Glc-6-P), but the majority is released into the portal blood.

The metabolic fate of fructose is its involvement in glycolysis, for which two pathways with different organ localization are used.



- ws:Metabolismus fruktózy (FBLT)

The fate of fructose in the body

Fate of fructose in the liver

On the one hand, fructose is very quickly absorbed by the liver, where it is also metabolized using the enzyme "fructokinase" specific for fructose phosphorylation. Now let's look at the corresponding reaction:

Fructose + ATP → fructose-1-P + ADP

catalyzed by fructokinase

Fructose-1-P is not an intermediate product of glycolysis and its further transformation is catalyzed by the so-called *aldolase B* (different from aldolase A in glycolysis).
The cleavage of Fructose-1-P produces two trioses – glyceraldehyde and dihydroxyacetone phosphate.

- '*Dihydroxyacetone phosphate* can be immediately involved as an intermediate of glycolysis.
- '*Glyceraldehyde* has a more complicated fate. It can be phosphorylated by a specific kinase to *glyceraldehyde-3-phosphate*, or it can be reduced to *glycerol*.

  Phosphorylation is much more important, as it serves to connect glyceraldehyde to glycolysis.

Fructose-1-P' → dihydroxyacetone phosphate' + D-glyceraldehyde

catalyzed by specific aldolase B

Dihydroxyacetone phosphate' → glyceraldehyde-3-P' → glycolysis

D-glyceraldehyde' → glyceraldehyde-3-P' → glycolysis

or → **glycerol → glycerol-3-phosphate' → triacylglycerols**

There is a very rare congenital defect of aldolase B that causes a disease called fructose intolerance, in which Fru-1-P accumulates, resulting in an imbalance in carbohydrate metabolism.

Fructose metabolism is **faster'** than glucose metabolism, as the main regulatory (slowest) step of glycolysis catalyzed by *phosphofructokinase* is bypassed.
As a result, this can lead to increased hepatic lipogenesis – from the excess pyruvate (and subsequently AcCoA) produced, an excessive amount of fatty acids and triacylglycerols are produced.

Alternative fate of fructose

To a lesser extent and also in other tissues (e.g. muscles) fructose is phosphorylated by *hexokinase*:

Fructose' + ATP' → Fructose-6-P' + ADP

The resulting Fructose-6-P is a direct intermediate product of glycolysis, and the route of connecting fructose therefore takes much less time.
However, hexokinase has a higher K_m for fructose and thus a low affinity.

Importance of fructose for sperm

Sperms use fructose as their **main source of energy**.

Therefore, it is not surprising that there is a very high concentration of fructose (5-10 mmol/l) in the seminal fluid, which is produced by the seminal glands from glucose.

First, glucose is reduced to sorbitol, which is then oxidized to fructose.

Metabolism of galactose

Metabolism of galactose

Galactose Metabolism

Conversion of glucose to galactose

Galactose is used in the human body for the synthesis of lactose in the lactating mammary gland or in the formation of glycoproteins, proteoglycans and glycolipids.
As mentioned above, the interconversion of glucose to galactose (and back) does not take place in the form of free carbohydrates. These must be activated first.
After the activation of glucose to UDP-1-glucose , its isomerization to UDP-galactose occurs :

UDP-1-glukose ↔ UDP-galaktose

(catalyzed by 4-epimerase)

The formed UDP-galactose is a macroergic compound and can be directly used for the synthesis of the aforementioned compounds.

Lactose synthesis takes place **only in lacting mammary gland**.
It combines UDP-galactose with glucose (catalyzed by galactosyltransferase).
Lactation is supported by prolactin – a peptide hormone from the adenohypophysis.

Conversion of glucose into glucuronic acid and its use

Conversion of glucose to glucuronic acid and its use

Use of Glucuronic Acid

Utilization of glucuronic acid