Adenosine triphosphate is a purine nucleotide with three phosphate groups connected to a carbon ring. It provides energy to all cells of the human body. It is derived from phosphorylation of ADP. ATP is needed as the storage form of energy needed for cellular respiration. Understanding how ATP can be synthesized, and how it is used by the body, forms a fundamental part of pre-med biochemistry.

The Chemical Properties of Adenosine Triphosphate (ATP)

ATP is a purine nucleotide that has three phosphate groups connected to the 5’-carbon of the ribose ring. It is composed of the following parts:

- Adenine: a purine base
- Ribose: a 5-carbon sugar ring
- Triphosphate: three phosphorous groups
Adenine and ribose form together a nucleoside called adenosine. If they are connected to three phosphorous groups, the resulting structure is called adenosine triphosphate (ATP). The purine base is connected to the ribose’s 1’-carbon via an N-glycosidic bond. An ester bond connects the triphosphate group with the 5’-carbon of the ribose.

ATP’s high energy content is contained in the anhydride bond of the triphosphate group. In the hydrolysis of ATP to adenosine diphosphate (ADP) at standard state, the anhydride bonds are cleaved and release approximately 30.5 kJ/mol. When ADP is further hydrolyzed to adenosine monophosphate (AMP), another anhydride bond is cleaved, and another 30.5 kJ/mol are released at standard state.

It is also possible to directly convert ATP to AMP by cleaving a pyrophosphate unit from ATP. Under the typical conditions in a human cell, however, the energy release is approximately 50 kJ/mol!
Synthesis of ATP

In the entire metabolic system, there are four reactions that generate high-energy nucleoside triphosphates (ATP or GTP = guanosine triphosphate). In cellular respiration, ATP is produced from ADP through oxidative phosphorylation. In glycolysis and the citric acid cycle, the phosphate is added to ADP through substrate-level phosphorylation.

Cellular respiration
The central functional component of cellular respiration is **ATP synthase**, an enzyme consisting of two parts: The catalytic head part (the F1 portion) projects into the matrix of the mitochondrion and is connected to the F0 portion, which is a proton channel embedded on the **inside of the mitochondrial membrane**.

The **energy needed for the synthesis of ATP comes from a proton gradient** across the inner mitochondrial membrane, which is generated by the **four preceding respiratory chain complexes** (H⁺ concentration in the intermembrane space > H⁺ concentration in the matrix). Due to the gradient-directed passing of H⁺ ions through the F0 portion of the ATPase, the catalytic center of the F1 portion experiences a change in conformation. Bound ADP is phosphorylated to ATP.

This entire process is called **oxidative phosphorylation** because the **energy** needed to generate the proton gradient **comes from the redox reactions of the four respiratory chain complexes**. For these redox reactions, NADH+H⁺ and FADH₂ are needed, which are provided by glycolysis and the citric acid cycle.

**Substrate-level phosphorylation**
The process of substrate-level phosphorylation occurs during glycolysis and the citric acid cycle. **Substrate-level phosphorylation** uses the energy released from reactions of a metabolic pathway (substrate level) to transfer an inorganic phosphate group from a substrate to ADP or GDP.

During **glycolysis**, the following reactions yield ATP from ADP:

- \(1,3\text{-bisphosphoglycerate} + \text{ADP} + \text{P}_i \rightarrow 3\text{-phosphoglycerate} + \text{ATP}\): This reaction is catalyzed by phosphoglycerate kinase.
- \(\text{Phosphoenolpyruvate} + \text{ADP} + \text{P}_i \rightarrow \text{pyruvate} + \text{ATP}\): This reaction is catalyzed by pyruvate kinase.

For more information, see: [Glycolysis - Energy Metabolism](#).

In the **citric acid cycle**, GTP is synthesized from GDP. GTP is similar to ATP regarding its energy content:

- \(\text{Succinyl-CoA} + \text{GDP} + \text{P}_i \rightarrow \text{succinate} + \text{GTP} + \text{CoA}\): This reaction is catalyzed by succinyl-CoA synthetase.

**Energy balance**

In sum, one can calculate how many ATP molecules can be generated from one mole of glucose. Such a calculation is based on the assumption that **one NADH yields 10 protons and one FADH\(_2\) yields 6 protons for the creation of the proton gradient of cellular respiration. For the synthesis of 1 ATP from ADP + P\(_i\), a flow of 4 protons across the inner mitochondrial membrane is needed**, meaning that 1 NADH can produce 2.5 ATP, and 1 FADH\(_2\) can produce 1.5 ATP. This results in the following high-energy compounds generated from 1 mole of glucose:

- **Glycolysis**: 2 ATP + 2 NADH → 7 ATP
Pyruvate dehydrogenase: $2 \text{ NADH} \rightarrow 5 \text{ ATP}$

Citric acid cycle: $6 \text{ NADH}, 2 \text{ FADH}_2, 2 \text{ GTP} \rightarrow 19 \text{ ATP}$

**Total:** 31 ATP

However, because **1 ATP is used by the glycerophosphate shuttle**, which transports NADH from glycolysis to the cellular respiration of the mitochondria, **1 mole of glucose yields 30 moles of ATP!**

**References**


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