Caffeine

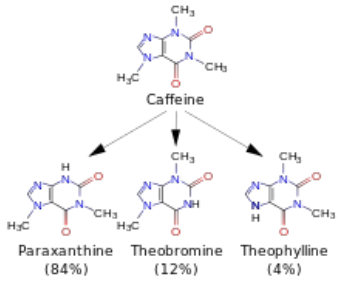
Caffeine or 1,3,7-trimethylxanthine is a purine alkaloid belonging to the group od methylxanthines. It influences the function of the cardiovascular, respiratory, renal and nervous systems. It has several mechanisms of action. Caffeine is among the **most widespread and used** stimulants in the world. The sources of caffeine are coffee and cocoa beans, tea tree leaves or guarana berries, glossy kola (or real kola), Paraguayan holly and several other plants.

Chemical properties

- General formula: $C_8H_{10}N_4O_2$
- Molar mass: 194,19 g/mol
- Melting point: 235-238 °C
- Density: 1,2 g/cm^3
- UV maximum: 275 nm
- Biological half-life (in plasma): 3-7 hours
- Total plasma clearance: 0,078 L/h/kg
- Properties: white crystal or powder, odorless, slightly bitter taste. [1].

Caffeine metabolism

About 99% is absorbed during digestion i**n the first 45 minutes**. If it enters the body in the fluidal form, absorption takes place in the GIT (stomach and small intestine) and is distributed using body fluids. In the case of chewing various plant leaves, absorption is faster and already takes place in the area of the oral mucosa. It can reversibly bind to plasma proteins (approximately 10-30%). Caffeine is resorbed in the renal tubules, but most is filtrated by the glomerulus and only a small percentage is excreted unchanged in the urine.



Metabolites of caffeine

Caffeine metabolism itself takes place in the **liver**. Many enzymatic systems are involved, especially **cytochrome P450** enzymes (in the form N-demethylation), N-acetyltransferase (NAT), xanthine oxidase (XO), etc. Demethylation and oxidation produce the **three most important metabolites** of caffeine:

- **paraxanthine** is a metabolic product of roughly 80-85% of the total volume of caffeine; it causes increase of lipolysis, which leads to an icrease in plasma concentrations of glycerol and free fatty acids;
- **teobromine**: about 12% of the total volume of caffeine; it dilates blood vessels and increases urine volume;
- **teophylline**: arounnd 4% of the total volume of caffeine and it leads to relaxation of the smooth muscle in the bronchus

Mechanism of action

Several metabolic pathways through which coffeine acts have been described. However two are most important: inhibition of phosphodiesterase and antagonism of adenosine receptors. It also includes the release of calcium from intracellular resources or antagonism of benzodiazepine receptors.

1. **Inhibition of phosphodiesterase:** Caffeine inhibits phophodiesterase (an enzyme, that catalyzes the hydrolysis of cAMP), leading to an increase in cAMP concentration. Thus, caffeine indirectly affects the regulation of cAMP-dependant protein kinases, which are responsible for the regulation of glycogen, sugars and lipid metabolism. By activating hormone-sensitive lipases, the lipolysis increases, which is manifested by an increase in plasma levels of free fatty acids and glycerol. There is also an increased release of catecholamines.
2. **Adenosine receptor antagonism**: It has major effect on bahavioral and cognitive functions. Caffeine binds non-specifically to adenosine receptors. The cells are then "blind" to adenosine. When adenosine binds to its receptors, it acts as an inhibitor of nerve signals, which leads to drowsiness, lethargy, and sleep. Furthermore, adenosine dilates the blood vessels of the brain. By binding caffeine a paraxanthine to adenosine receptors, opposite reactions occur: acceleration of nerve signals, a feeling of alertness and constriction of cerebral vessels.

Effects

- Acceleration of psychomotor skills
- Alleviation of fatigue
- Palpitation
- Improving concetration and memory
- Greater use of fat as an energy source
- Diuretic effect

At higher doses, tachycardia, hypertension, nausea, anxiety, inability to concentrate, tremors or involuntary muscle twitches may occur.

Dependence

Caffeine is one the **least addictive** drugs, yet its overuse can cause addiction. However its use is relatively safe, as the lethal dose for a healthy invidual is around 10 grams (about 100 cups of coffee). If the caffeine intake is reduces or discontinued after long-term regular use of higher doses, **withdrawal symptoms** may occur. These are not usually strong, they include irritability, fatigue, dysphoria. They disappear within 2-3 days. About 300mg of caffeine (3 cups of coffee) is considered as a relatively safe dose.

Links

Related articles

- Addictive substances
- Substance abuse

References

1. UNIVERSITY OF DELAWARE,. *The Chemistry of Caffeine* [online]. [cit. 2013-04-19]. <http://www1.udel.edu/chem/C465/senior/fall00/Caffeine/Chemistry.htm>.