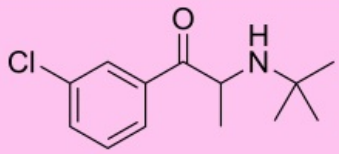
Bupropion

Bupropion, alternative name amfebutamone, is a prototype **IV antidepressant**. **generation**, because it increases the concentration of 2 out of 3 monoamines in the synaptic cleft. It interferes with the dopaminergic and noradrenergic system of the CNS and increases the concentration of dopamine and noradrenaline in these synapses in a not completely explained way. This dual-acting antidepressant is primarily indicated for **depressive disorder and smoking cessation** . In addition, there are also a number of off-label uses based on smaller studies and case reports. Unlike other antidepressants, it is well tolerated, it is also suitable as a drug of first choice, it does not affect sexual function or body weight. On the contrary, thanks to its considerable similarity to amphetamines **has an activating effect and reduces appetite**.

Bupropion	
BUPROPION HYDROCHLORIDE	
N06AX12	
	
Bupropion chemical formula	
Onset of effect	weeks
Elimination	hepatic metabolism; the half-life for Bupropion is 20 hours
Indication	treatment of depression ; smoking cessation
Contraindication	epilepsy , insomnia , anxiety disorders , suicidal behavior , self-harm , anorexia nervosa , bulimia , liver insufficiency
Side effects	convulsions , nausea , cephalgia , dryness of mucous membranes , insomnia
Interaction	inducers and inhibitors of CYP2B6
Systematic name	(±)-2-(*tert* -Butylamino)-1-(3-chlorophenyl)propan-1-one

Pharmacology

Pharmacodynamics

Bupropion is characterized as a **dopamine-norepinephrine reuptake inhibitor** (NDRI). Based on animal and in vitro studies, in addition to inhibiting the reuptake of the mentioned mediators, it is also able to act on the presynaptic terminal and thus release dopamine and noradrenaline from storage vesicles. It also acts as **an indirect sympathomimetic** . When metabolizing, it is heavily burdened by the first-pass effect and changes into its active metabolites. The most important of them is hydroxybupropion, a selective noradrenaline reuptake inhibitor and nicotinic receptor antagonist.

However, hydroxybupropion does not show dopaminergic transmission enhancing activity. Bupropion and some of its other metabolites appear to be directly responsible for the dopaminergic effects. These probably bind to and **block the dopamine transporter** (DAT), whose function is to transport dopamine from the synaptic cleft back into the cytosol. This blockade increases dopamine levels. By blocking the dopamine transporter, it strongly resembles cocaine (cocaine-like effect), which, however, blocks the transporter excessively excessively. For this mechanism of action, the use of bupropion by snorting or intravenously has occurred in several countries. Bupropion therefore has some potential for abuse.

It acts as a **non-competitive antagonist** on nicotine receptors , which is why it is used both in smoking cessation and in the treatment of depression.

Pharmacokinetics

Bupropion is metabolised mainly in the liver by cytochrome P450 (or its isoenzyme CYP2B6) into three substances, whose concentration in the blood and cerebrospinal fluid exceeds the concentration of bupropion itself. The three metabolites are hydroxybupropion, threohydroxybupropion and erythrohydroxybupropion, with the above-mentioned hydroxybupropion being the most important. The maximum plasma concentration in the blood is usually reached within 3 hours after administration. Bupropion and its metabolites are mainly excreted in urine (around 87%) and the rest in faeces. The elimination half-life is approximately 20 hours, and bupropion and its metabolites reach steady plasma concentrations within 8 days.

Use in medicine

Treatment of depression

Thanks to the fact that bupropion has significantly expressed activating effects, it is very suitable for depressive disorders, where the leading symptom **is a dislike for life, somnolence and psychomotor depression** . It appears to be more effective than conventional SSRIs (sertraline, escitalopram or paroxetine, etc.) in these patients. These are more suitable for the anxious form of depression. A number of observations have shown that bupropion is also effective in severe depression and can even be combined with other antidepressants (most commonly sertraline and fluoxetine) if patients do not respond sufficiently to SSRI treatment.

Quitting smoking

Due to the increase in dopamine and noradrenaline levels, bupropion **suppresses cravings** and **withdrawal symptoms** after nicotine withdrawal. The anticraving effects are explained by increased dopamine, the suppression of withdrawal symptoms by increased noradrenaline. Typical bupropion therapy lasts from 7 to 12 weeks. After stopping treatment, bupropion approximately doubles the chance of quitting smoking within the next

3 months. In the next year after stopping treatment, the chance of quitting smoking is still 1.5 times higher than for people who did not undergo bupropion treatment. In addition to dopamine and noradrenaline, the antagonism of hydroxybupropion on α 4 β 2 nicotinic receptors is also responsible for smoking cessation.

Sexual dysfunction

When taking common antidepressants, the dreaded side effect is the suppression of sexual functions. Bupropion does not have these side effects, and on the contrary, augmentation of SSRIs with bupropion has been shown to lead to a statistically significant **improvement in libido and frequency of sexual intercourse** . Recently, it has also been tested in non-depressed patients with sexual dysfunctions. Its use appears promising in women with reduced libido and the ability to achieve orgasm.

Off-label use

A 2006 study showed that bupropion shows some effectiveness in other indications than just treating depression or smoking cessation. The study proves its successful use in patients with ADHD , restless legs syndrome , chronic fatigue syndrome , and from somatic diseases , rheumatoid arthritis , Crohn's disease , multiple myeloma and chronic lymphocytic leukemia[1] . An interesting fact is that bupropion, like its similar amphetamines, suppresses the appetite. A 2005 study found that after 6 to 12 months of taking bupropion, patients lost around 2.7 kg . However, this weight loss is not very different from conventionally used anorectics such as sibutramine or amfepramone.

Contraindications

They result from its activating and anorectic effects. Due to its ability to stimulate the CNS, it is not recommended for **epilepsy** , insomnia , anxiety states and suicidal behavior or self-harm (it gives confidence to do something). Due to its anorexic effect, it is not recommended for anorexia nervosa and bulimia nervosa . Concomitant use of MAO inhibitors or withdrawal from alcohol or benzodiazepines is also contraindicated. Of the somatic contraindications, these are disorders of liver or kidney function.[2]

Side effects

They are not very common. **Headache, dry mouth, dizziness, nausea and insomnia** are most often described . The most serious side effect is **the risk of epileptic seizures** . The risk is strongly dependent on the dosage method. A single dose of up to 300 mg has a risk of 0.1%, while a dose of 450-600 mg has a risk of 5%. The problem can be elegantly solved by using a sustained release dosage form.

Drug interactions

Bupropion is metabolized in the liver by CYP2B6. This isoenzyme is inhibited in the body by several other drugs, which then result in bupropion not being fully saturated by the enzyme and thus reducing the concentration of the desired metabolite hydroxybupropion in the plasma. These inhibitors include, for example: paroxetine, sertraline, fluoxetine, diazepam or clopidogrel. Isoenzyme inducers are, for example: carbamazepine, rifampicin , phenobarbital or phenytoin. Analogously, these inducers will, on the contrary, cause an increase in the plasma concentration of active hydroxybupropion. The result is a more pronounced expression of the effects (and side effects) of bupropion.

Indications in the Czech Republic

Bupropion was registered in the Czech Republic in 2001. Its indications are depressive disorder and smoking cessation. It is available by prescription as extended-release tablets under the trade names **Wellbutrin** or **Elontril** (BUPROPION-HYDROCHLORIDE). The initial dose is usually 150 mg once a day. In case of insufficient response to treatment, the dose can be increased to the usual 300 mg per day. The dose can be increased up to a maximum of 400 mg/day.

Links

Related Articles

- Antidepressants
- Depression

References

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