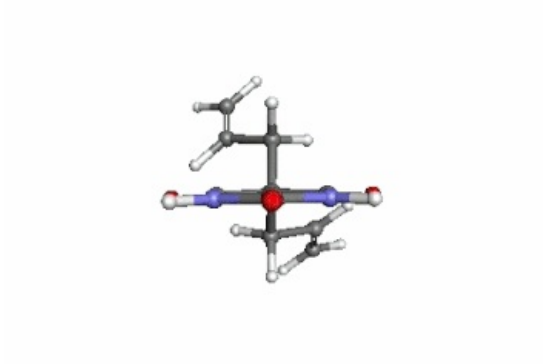
Sedatives

Sedatives (formerly called *tranquilizers*) are substances with a depressant effect on the CNS. They also often have a hypnotic effect and in many cases(benzodiazepines and barbituates) also an anxiolytic effect. Depending on the dose, they usually have a sedative, hypnotic or general anesthetic effect.

Representatives

A number of those listed below are already obsolete or banned, but their use, or patients suffering from the consequences of their use, can still be encountered. Sedatives can be of natural or synthetic origin. Doležel et al. (2013) and Lüllmann (c2002) distinguish the following groups of sedatives from a pharmaco-chemical point of view:

- melatonin receptor agonists (melatonin),
- alcohols and their functional derivatives (chloral hydrate, chlorobutanol),
- aliphatic amides and ureides – barbiturates



3D model molecule barbituates

Note: Barbiturates are rather obsolete today, they are important in invasive procedures under general anesthesia. They are not used in outpatient practice because of their small therapeutic range. No antidote is available in case of overdose. Use is accompanied by a high risk of addiction. Lullmann et al. although he describes the risk of addiction as slight, which is contrary to the experience of most other authors

- benzodiazepines,
  - 7-nitrobenzodiazepine (nitrazepam, flunitrazepam),
  - imidazo- and triazolobenzodiazepines (midazolam),
  - N1-alkylbenzodiazepines (cinolazepam),
- derivatives diphenylmethane (hydroxyzine),
- derivatives propanediol (guaifenesin),
- hypnotics of other structures (sodium oxybate, clomethiazole)
- substances of natural origin (hops, lemon balm, valerian, St. John's wort),
- non-benzodiazepine hypnotics , the so-called "Z" hypnotics listed below are benzodiazepine analogues, but unlike benzodiazepines, they bind specifically to the gabaergic ω-receptor,
  - imidazopyridines (zolpidem),
  - pyrazolopyrimidines (zaleplone),
  - cyclopyrrolones (zopiclone, eszopiclone),

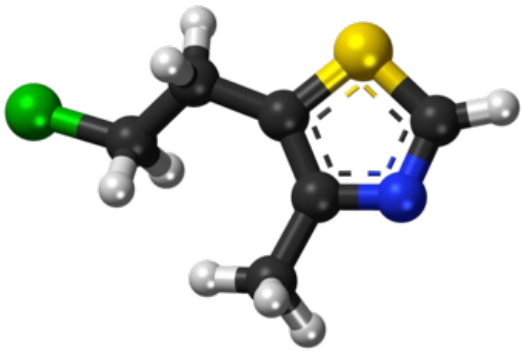
Of course, other drugs can also have a sedative effect. Typically some antidepressants (trazodone, mirtazapine, agomelatine), typical and atypical antipsychotics (haloperidol, quetiapine), antihistaminic (diphenhydramine, doxylamine) or some anticonvulsants.

Pharmacodynamics and pharmacokinetics

The site of action of most sedatives is the GABA-receptor complex. The mechanism of action of barbiturates and alcohols consists in prolonging the opening of the ion channel, or (in higher doses) they support its opening directly.

Benzodiazepines also allosterically bind to GABAergic, specifically GABA A receptors, where they potentiate the effect of GABA. The mechanism is to increase the frequency by opening the ion channels, not by increasing their opening interval.

Heminevrin (active substance has clomethiazole) significant sedative, hypnotic and anticonvulsant effects caused by the mechanism of increasing the transmission of GABA as an inhibitory mediator in the CNS. This results in a reduction in the generation of electrical stimuli in the CNS (used mainly in the therapy of delirium tremensand gerontological patients with cerebral vascular sclerosis.



Model molecule clomethiazole

Hydroxyzine acts on several types of receptors, including antagonistic to H1-receptors, it is also used as a relatively safe (in terms of habit potential) anxiolytic, which is probably due to anti serotonin effects.

Using

Due to the already mentioned anxiolytic and hypnotic (possibly anticonvulsant) effects, sedatives are used in a wide range of indications. They are, for example: premedication before surgery → for an anxiolytic effect during examination when the patient is conscious and for an overall narcotic effect during more extensive invasive procedures; insomnia; anxiety disorders; ; restlessness, agitation, excitement, increased psychomotor pace; intoxication with psychostimulant substances (**CAVE** : paradoxically, the patient can be excited even with intoxication with substances suppressing the activity of the CNS - there is a risk of mutual potentiation and suppression of respiratory functions or the activity of the

⚠**Most sedatives with a rapid onset of action show a relatively rapid increase in tolerance and the development of dependence, so their use should be limited to as short a time as possible. Alternatively (with long-term administration) it should be discontinued very slowly to avoid the rebound phenomenon.**

Links

Related Articles

- Benzodiazepines
- Hypnotics

External links

- Sedativum (česká wikipedie) (https://cs.wikipedia.org/wiki/Sedativum%7C)

Sources

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