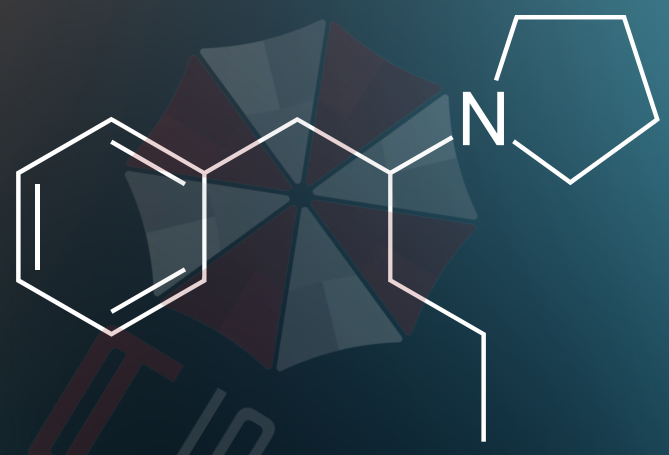

Pharmacological Profile and Metabolism of Prolintane: A Review

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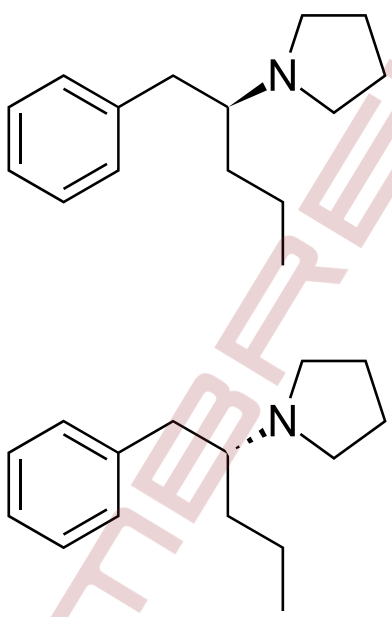
History

Prolintane (Katovit) was developed in the early 1950`s by the predecessor of Böhringer-Ingelheim, then still called the Dr. Karl Thomae GmbH, which filed a patent in 1955. It is a mixture of 2 Enantiomers, (S)-Prolintane and (R)-Prolintane, which are usually not separated. As a distant structural relative to amphetamines, it possesses stimulating properties.



(S) and (R) Prolintane

It was sold under the brand name Katovit the EU until 2001. In the US, it never had the status of an approv. Today, it is sometimes used in doping.[1] It is included in the prohibited list of the Wold-Anti- Doping Agency.

The synthesis of prolintane has been described via several routes, [2] one new route was published as of 2025.[3]

Mechanism of Action

Prolintane is a central nervous system stimulant and norepinephrine–dopamine reuptake inhibitor (NDRI).

Animal Experiments

A study in mice at a dose of 20 mg/kg (i.p.) showed increases locomotor activity in a lesser degree than methamphetamine. An injection of prolintane results a significant increase in extracellular dopamine in the brain area of the striatum. The results also indicated that prolintane has rewarding and reinforcing effects on the brains of the animals, indicating potentially addictive properties in humans.[4]

In a different study in mice and rats, prolintane seemed to affect the brain's immune cells and possibly disrupted communication between brain cells. Although it didn't damage heart muscle cells, prolintane may lead to dangerous heart rhythm issues by interfering with a key heart-related protein (hERG).[5]

Analysis

Two studies investigated the detection of prolintane metabolites in human urine by HPLC and GC due to its potential in doping.[6,7]

Metabolism.

In rats, 57% of prolintane metabolites are excreted within 48 h hours at a dose of 50 mg/kg (i.p.). A pyrrolidine ring-opened metabolite (15% dose) and p- hydroxyprolintane (5% dose) were excreted as predominant metabolites together with traces of unchanged chemical and oxoprolintane. The stud also suggested the 2 metabolites p-hydroxyprolintane and (ω-1)-hydroxyprolintane also have biological activity.[8]

Rabbits receiving the chemical in oral dose of 270 mg/kg or 170 mg/kg excreted seven metabolites together with a trace of unchanged chemical in the 24 hr urine. They were shown to be lactam, phenol, alcohol, lactam phenol, two diastereoisomeric lactam alcohols and amino acid, by infrared, nuclear magnetic resonance and mass spectra.[9]

When prolintane hydrochloride was supplied in racemic form and in the forms of both enantiomers to volunteers found that the compound is primarily hydroxylated in the liver to form various metabolites. The 5-membered pyrrolidine ring can be opened by further oxidation. The metabolism of the enantiomers differs mainly in the quantitative amounts of metabolites.[10]

Clinical Trials

In one study, 24 healthy fatigued volunteers received 10 and 20 mg of prolintane, which was compared to a dose of 10 mg amphetamine. Prolintane appeared to be a much milder stimulant than dextroamphetamine. While it produced fewer sympathomimetic effects than dextroamphetamine, this difference might not necessarily hold at equivalent stimulating doses. Like other weak stimulants, such as methylphenidate and pipradrol, the major differences from dextroamphetamine were quantitative rather than qualitative.[11]

Another clinical study looked at the sleep impact of various stimulants on human sleep. 5 or 10 mg of prolintane hydrochloride reduced REM activity in the first 2 h of sleep, but there were no other changes in sleep. The subjects as a group reported that they slept less well with the higher dose, but sleep onset and wakefulness the next morning were not altered.[12]

The effects of prolintane (15 and 30 mg) and pemoline (60 and 100 mg) on sleep were further studied in six healthy adult males. Prolintane (15 and 30 mg) reduced rapid eye movement (REM) sleep both by delaying the first period and by reducing total REM sleep. In some subjects there were increased awakenings during the early part of the night, and in two subjects long periods of wakefulness occurred.[13]

In a case study, the combination of prolintane with the anti-histaminergic chemical diphenhydramine induced visual hallucinations in a young man in 2002.[14]

Conclusion

Due to the long time since the first studies of prolintane have been conducted in humans, many of them are not available.

It is generally regarded as a milder form of amphetamines with somewhat limited stimulating effects (increased wakefulness and locomotor effects). In animal experiments, addictive behaviour was reported. There is not much data on the mechanism of the compound, but it is generally classified as norepinephrine–dopamine reuptake inhibitor.

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