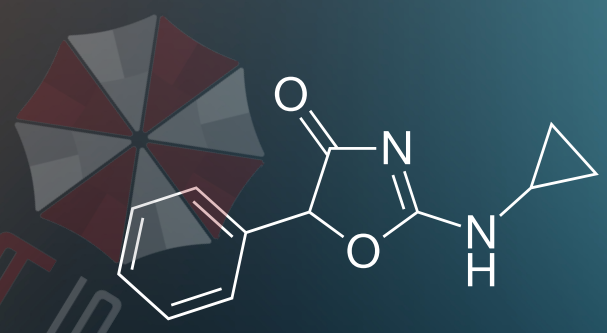


Cyclazodone - Reviving Research on a Forgotten Stimulant

History

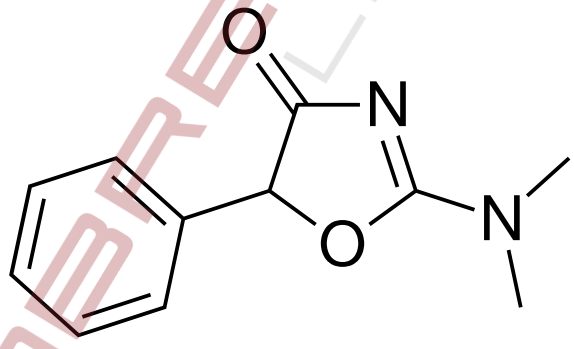
Cyclazodone was developed by the American Cyanamid Company in the 1960`s (Patent: US3321470A). It belongs to the group of aminorex analogues. Aminorex, which was initially marketed as medication for weight loss, became available to the market in 1965, but was withdrawn because it was found to cause pulmonary hypertension, a potentially deadly side effect of the drug. Concurrently with the development of Aminorex, other compounds with similar structures were developed and tested. Cyclazodone was then synthesized as a structural analog of the – at the time – already known compound thozalinone.

Compounds of the same group (including Cyclazodone) do cause increased wakefulness and reduced appetite, while it has little cardiovascular and sympathomimetic (sweating, increased blood pressure) side effects, especially when compared to the amphetamine group of stimulants. Another reason this group was thought superior over amphetamines for clinical is its reported absence of psychological dependence. Other derivatives like Thozalinone and showed a more favorable side effect profile. (Patent: US3609159A) From the alternatives to Thozalinone, Cyclazodone was found to be the most potent compound when injected in mice. Results showed at a dosage of 10 mg/kg bodyweight a strong excitatory effect which lasted longer than 6 hours with a maximum activity displayed between 120 and 180 minutes. Cyclazodone seems to be ca. 5 times stronger than Thozalinone (Patent: GB1005738A).

Overdosing Cyclazodone, Thozalinone or similar compounds may result in irregular and involuntary muscle contractions.

Pharmacology

However, Cyclazodone has never been used or trialed for use in humans, and with very few data reported on mice, the overall availability of data is very limited. While there is almost no pharmacological data available on Cyclazodone itself, there is somewhat more data for Thozalinone. As Thozalinone, which was used as an antidepressant in Europe, is the closest structural analogue of



Thozalinone

Cyclazodone, its effects will be briefly presented here.

In mice, Thozalinone increased searching behaviour, alertness and preening, as well as increase in general motor activity when administered orally at doses between 7.5 and 960 mg/kg bodyweight. 960 mg was determined as toxic levels characterised by a drop in locomotor behaviour and death. Lethal dosages for cats were reported at 250 mg/kg for dogs at 500 mg/kg. At these extreme dosages, some surviving animals did not accept food until several days after administration. A general decrease in food intake was already observed at much lower dosages around 16 mg/kg. It was also reported to be able to counteract effects of sedating drugs like pentobarbital. No increase in body temperature, blood pressure, heartrate was reported at regular doses.[1]

There are reports of human studies with Thozalinone (Sources [2] and [3]), due to their age, they seem not to be available publicly unfortunately.

Doping Uses

Since Cyclazodone is included in the World Anti-Doping Agency prohibited list, there a few studies that demonstrate the detection of Cyclazodone from urine with either HPLC-MS[4] and or GC-MS.[5]

Conclusion

From the available data, it can be- with a certain degree of uncertainty-concluded that Cyclazodone is a more active alternative to Thozalinone. In general, it could be expected that the same results (and toxicity) could be achieved be reducing the equivalent Thozalinone dose by 80%.

Potential uses of Cyclazodone seems to be short-term only, either for increased locomotor activity during intense exercise, for weight loss or its antidepressant effects, although there are better alternatives like modern SSRI´s for this indication.

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