

FIRST REPORT ON BRORPHINE: THE NEXT OPIOID ON THE DEADLY NPS' HORIZON?

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BACKGROUND

New psychoactive substances (NPS) continue to appear on the drug market. Until recently, new synthetic opioids, which are amongst the most dangerous NPS, primarily encompassed analogues of the potent analgesic fentanyl. Lately, also other new synthetic opioids have increasingly started to surface.

This is the first report on the identification and full chemical characterization of online sourced brorphine, a novel potent synthetic opioid with a piperidine benzimidazolone structure. Brorphine was identified in a powder and in serum of a patient seeking medical help for detoxification. In addition, its μ -opioid receptor (MOR) agonistic activity was demonstrated.

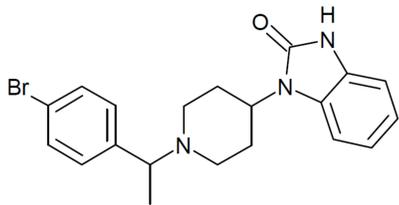


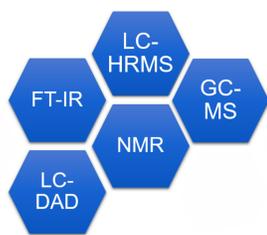
Figure 1. Chemical structure of brorphine.

CASE

- 24-year-old man
- querying admission for detoxification
- withdrawal symptoms
- generalized pain & weakness, confusion and cramping
- medical history of opioid misuse
- brorphine use four times a day orally
- "pretty strong effect with a long lasting high"

METHODS

- Chemical characterization:



- In-vitro biological activity by a cell-based MOR assay:



RESULTS

- LC-HRMS: m/z 400.1020 and 402.1005 \sim ⁷⁹⁻⁸¹Br isotopes (Figure 2)
- GC-MS, LC-DAD and FT-IR spectra
- NMR-analyses confirmed the structural configuration
- Bio-assay: EC_{50} = 30.9 nM \sim high potency (Figure 3)
- E_{max} = 209% (relative to HM) \sim high efficacy (Figure 3)
- Brorphine in 2 serum samples: 69.4 and 7.9 ng/mL
- Confirmation of opioid activity in serum via MOR assay

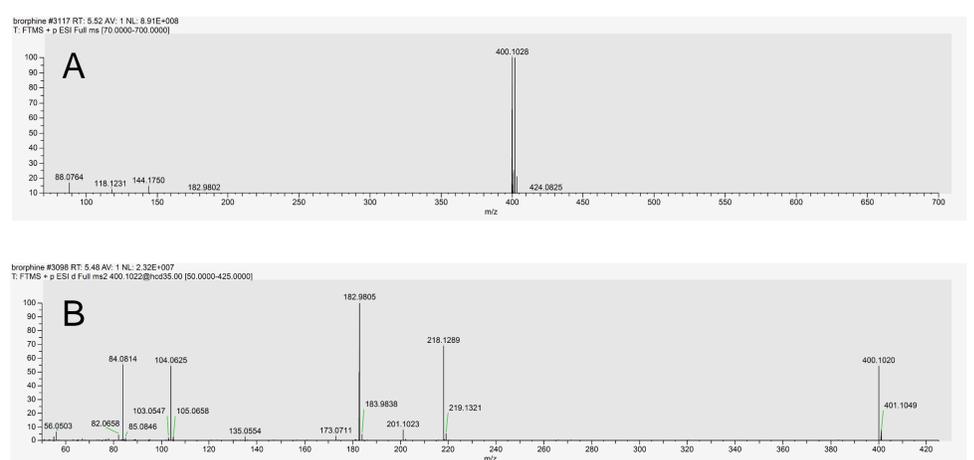


Figure 2. (A) HR-MS full scan spectrum. (B) HR-MS fragment ion spectrum.

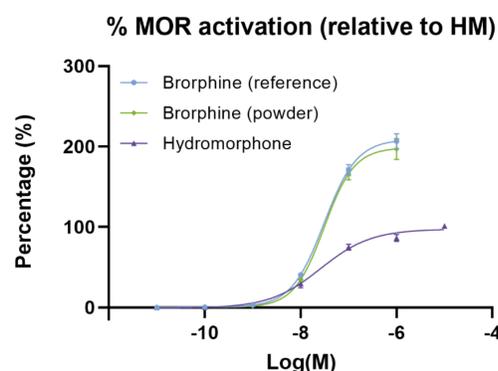


Figure 3. Concentration-dependent interaction of MOR with the brorphine reference standard, the obtained brorphine powder and the reference agonist, hydromorphone (HM). Data are normalized to the E_{max} of HM (=100%).

CONCLUSIONS

- The occurrence of brorphine is yet another example of how the illicit drug market is continuously evolving in an attempt to escape international legislation.
- The online availability of this compound, combined with its non-scheduled nature in many countries, its unequivocal identification in serum samples from a patient, and the demonstration that it acts as a strong MOR agonist: all these aspects should alert toxicology labs, as new cases - including fatalities involving brorphine - may emerge.

