

First report on brorphine: the next opioid on the deadly new psychoactive substances' 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.

Methods:

Chemical characterization of the powder was performed by liquid chromatography high resolution mass spectrometry (LC-HRMS), gas chromatography (GC)-MS, LC diode array detection (DAD), Fourier-transform infrared (FT-IR) and NMR spectroscopy analyses. *In vitro* biological activity of brorphine was determined by a cell-based μ -opioid receptor (MOR) activation assay. Patient samples were analyzed with the same LC-HRMS method and the bio-assay.

Results:

LC-HRMS identified an exact mass of m/z 400.1020 and 402.1005 for the compound, corresponding to both bromine isotopes. GC-MS, LC-DAD and FT-IR spectra were obtained from the powder. Structural confirmation was obtained using ¹H- and ¹³C-NMR analyses. An EC₅₀ of 30.6 nM (13.4 ng/mL) and an E_{max} of 213% relative to hydromorphone, were derived from the bio-assay, confirming the high potency and efficacy of this compound. The potency of brorphine approaches that of the potent analgesic fentanyl (18.7 nM). In a serum sample of the patient, brorphine and a hydroxyl metabolite were found using the LC-HRMS screening method. The presence of opioid activity in serum was confirmed via the MOR activation assay as well.

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 unequivocal identification of brorphine in a serum sample from a patient, along with the demonstration that it acts as a strong MOR agonist, render it likely that new cases - including fatalities - will emerge.

Key words: brorphine, new psychoactive substances (NPS), synthetic opioids, high resolution mass spectrometry (HRMS), μ -opioid receptor, bio-assay