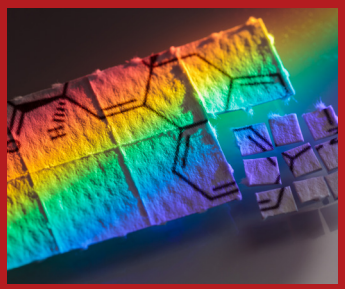
BMF 104 | 0124

CHIRON

NBOMes



N-Benzyl phenethylamines (such as NBOMes and NBOHs) are highly potent synthetic psychedelics, mimicking the effects of typical psychedelics such as LSD, mescaline and psilocybin. Following the initial detection of 25I-NBOMe, several structural analogues have appeared over the years. Exemplified by various case reports of severe intoxications and fatalities, NBOMes pose an important potential threat to public health and forensic toxicology labs should be aware of these harmful, emerging substances.

What are NBOMes?

N-Benzyl phenethylamines (NBOMes) are a class of new psychoactive substances (NPS) that have entered the recreational drug market since the 2010's. As synthetic psychedelics, they are highly potent serotonergic substances, derived from structures initially described by Alexander Shulgin.

Users of psychedelics typically chase mystical experiences and altered consciousness, however, compared to LSD, mescaline and psilocybin, NBOMes in particular have been associated with severe adverse events.

Serotonergic psychedelics have the serotonin 5-HT2A receptor as their main pharmacological target, and the relatively 5-HT2A selective NBOMes were initially synthesized with the aim to investigate the receptor's characteristics and distribution.

Since the first detection of 25I-NBOMe on the recreational drug market in Sweden in 2012, their popularity rose due to their wide availability online. Similar to substances described by Shulgin, several structural NBOMe analogues have emerged, with the iodine group of 25I-NBOMe being switched for another functional group such as a bromine (25B-NBOMe), chlorine (25C-NBOMe) aliphatic group (25E-NBOMe, 25D-NBOMe) and so on.

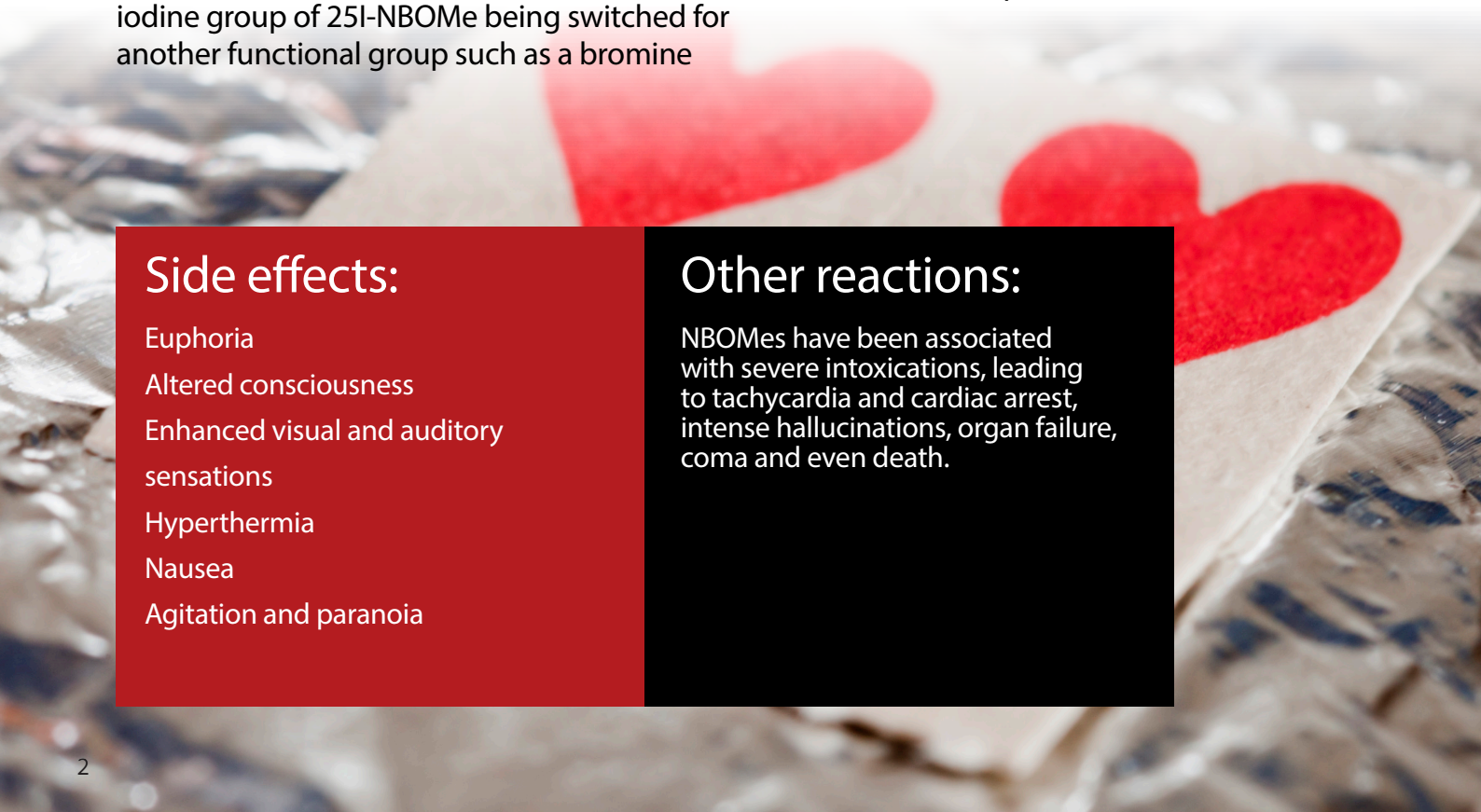
Furthermore, compounds with modifications at the N-benzyl group, for instance a hydroxyl substitution instead of the methoxy group, as is the case for 25I-NBOH, have appeared on the market.

Routes of administration

NBOMes are most commonly found on blotting papers, on which individual doses are absorbed and which are often decorated with colourful designs or images of cartoon characters. They have also appeared in liquid and in powder form.

NBOMes have been advertised as legal alternatives to LSD. Due to their detection in blotters sold as LSD and tablets sold as ecstasy, there is a risk of accidental exposure of users to these highly potent substances.

The most common routes of administration include sublingual, buccal (blotter) and nasal (nasal spray or insufflation) administration, but injection, smoking or rectal administration have also been reported.[1]



Side effects:

Euphoria

Altered consciousness

Enhanced visual and auditory sensations

Hyperthermia

Nausea

Agitation and paranoia

Other reactions:

NBOMes have been associated with severe intoxications, leading to tachycardia and cardiac arrest, intense hallucinations, organ failure, coma and even death.

Project overview

The rapid emergence of NPS results in a lack of knowledge on the pharmacological properties of these compounds, leading to their harms being potentially underestimated.

The Laboratory of Toxicology at Ghent University, Belgium, has developed in-house in vitro receptor-based bioassays, which allow for the assessment of their intrinsic activation potential of NPS at their target receptor.

The principle of the assay is based on functional complementation of a split nanoluciferase enzyme. One inactive subunit is fused to the receptor of interest (in the case of NBOMes the serotonergic 5-HT_{2A} receptor), whereas the other subunit is linked to ß-arrestin2, a signaling protein recruited to the receptor upon activation.

This brings the two subunits in close proximity, resulting in restoration of the enzymatic activity and generation of a luminescence signal, which is recorded using a luminometer. Irrespective of the chemical structure of the compound, serotonergic activity will be recorded, therefore also allowing the pharmacological characterization of newly emerging, unknown compounds.

Pottie et al. reported on the development of this assay and the functional characterization of a series of NBOMe substances and some structural analogs. Compared to LSD, which was used to normalize the obtained data, NBOMe analogs showed a clear increase in 5-HT_{2A} receptor activation potential.[7] They acted as full agonists, with their efficacy exceeding 100%. Whereas the unsubstituted 25H-NBOMe showed a similar potency to LSD, all other analyzed analogs (25I-, 25B-, 25C-, 25D, 25E-NBOMe and 25I-NBOH) were found to be highly potent and efficacious. The identity of the substitution appeared to have limited impact on the receptor activation potential.[7]

Additionally, switching the methoxy group at the N-benzyl moiety for a hydroxyl group (25I-NBOH) does not seem to majorly affect 5-HT_{2A}R activity. Overall, as exemplified by the several case reports related to NBOMe use, this class of psychedelics entails an important health risk, which may potentially be associated with their pronounced 5-HT_{2A}R activation potential.[7]

During the investigation of potential non-serotonergic, off-target properties of this class of substances, their ability to activate the μ opioid receptor (MOR), the prime target of opioid analgesics, was evaluated using similar activity-based bioassays. As reported by Deventer et al., some substances carrying the typical NBOMe structure were able to weakly elicit MOR effects in vitro in a similar way as opioids activate the receptor.[8]

Overall, the generated data contribute to a more in-depth understanding of the properties of new substances, which is often lacking for rapidly emerging NPS. Furthermore, the off-target findings indicate that future compounds with the NBOMe chemical backbone and some structural modifications may appear on the recreational drug market as substances with a potential dual MOR/5-HT_{2A}R activity, further complicating the NPS landscape. The results of both studies may be valuable for drug policy makers and health care workers by informing them about the potential threats to public health and aiding in the prioritization of legal responses.

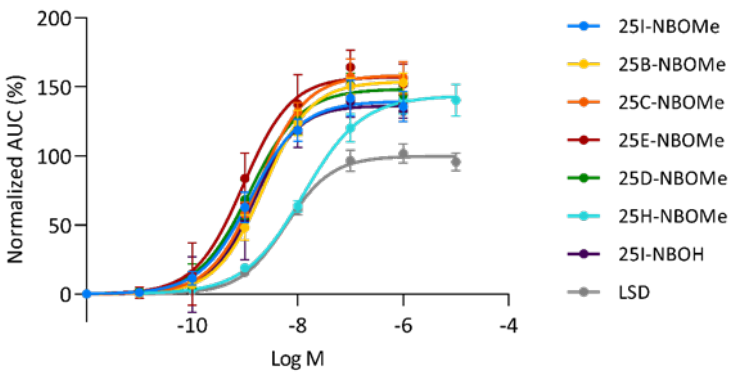


Image 1: Concentration-response curves of a set of NBOMe psychedelics, demonstrating activation potential at 5-HT_{2A}R.

International control status

Following the numerous reports of 25I-NBOMe-related poisonings and the subsequent risk assessment, the European Commission placed an EU-wide ban on the substance in 2014, although some nations had banned 25I-NBOMe prior to this measure.

25B-NBOMe, 25C-NBOMe and 25I-NBOMe are classified as Schedule I in the UN Convention on Psychotropic Substances of 1971. They were added to the International Narcotics Control Board (INCB) Green List (Psychotropic Substances under International Control) in 2015. Consequently several countries have placed bans on NBOMe analogues, for example Sweden has added 25I, 25B- and 25C-NBOMe as well as 25I-NBOH to Schedule I as narcotics. In 2023, Belgium adopted a generic legislation for the scheduling of NBOMes.

In the United Kingdom, all N-benzyl phenethylamines are listed as Class A, Schedule I drugs in the Misuse of Drugs Act 1971.

In the United States, as an emergency control measure, 25I-, 25B- and 25C-NBOMe were temporarily added to Schedule I followed by their permanent scheduling in 2016. Other analogues however are currently not controlled.[2-6]

About the authors

Dr. Eline Pottie graduated in 2017 as Master of Drug Development at Ghent University, Belgium. During her PhD research at the Laboratory of Toxicology, she focussed on the set-up and application of bioassays to monitor activation of G protein-coupled receptors (GPCRs). In 2022, she defended her PhD thesis entitled 'An enlightening trip through psychedelic and purinergic signalling'. As a postdoctoral researcher at the same lab, she now further investigates the in vitro pharmacology of psychedelic substances using different bioassays.

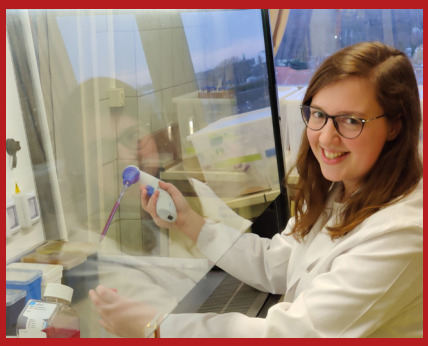


Image 1: Eline Pottie

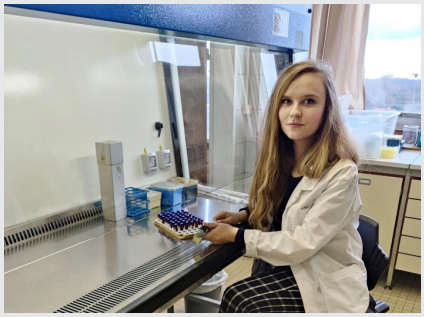


Image 2: Marie Deventer

Marie Deventer graduated in 2020 as Master in Pharmaceutical Care at Ghent University and started working as a PhD student in 2020 in the Laboratory of Toxicology under the supervision of Prof. Dr. Christophe Stove. She is currently doing research on alternative strategies for the characterization of and screening for new psychoactive substances.

NBOMes product listing

ISO 17034
ISO/IEC 17025
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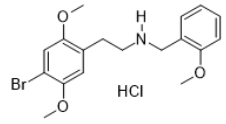
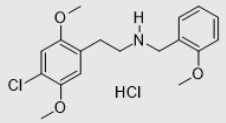
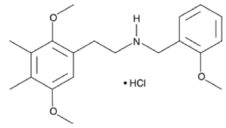
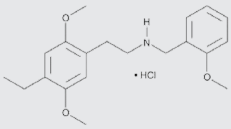
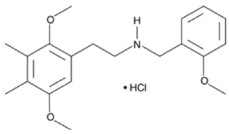
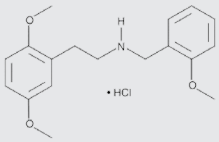
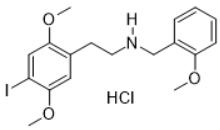
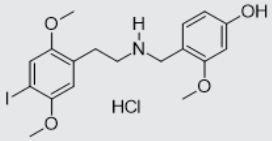
Chiron No.	Name	Structure	CAS
	NBOMes		
11366.18	25B-NBOMe hydrochloride (2C-B-NBOMe HCl)		1539266-15-3
10290.18	25C-NBOMe hydrochloride (2C-C-NBOMe HCl; 25C-NB2OMe HCl)		1539266-19-7
11457.19	25D-NBOMe hydrochloride (2C-D-NBOMe HCl)		1539266-35-7
11458.20	25E-NBOMe hydrochloride (2C-E-NBOMe HCl)		1539266-39-1
11466.20	25G-NBOMe hydrochloride (2C-G-NBOMe HCl)		1797132-54-7
11040.18	25H-NBOMe hydrochloride (2C-H-NBOMe HCl)		1566571-52-5
11299.18	25I-NBOMe hydrochloride (2C-I-NBOMe HCl)		1043868-97-8
11430.18	25I-NBOMe-M1 hydrochloride (2C-I-NBOMe-M1 HCl)		1800475-17-5 (free base)

NBOMes product listing

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Chiron No.	Name	Structure	CAS
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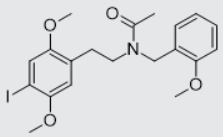
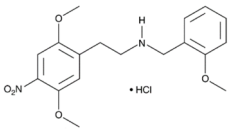
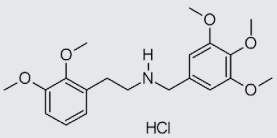
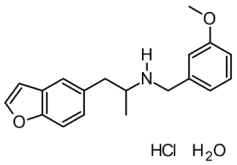
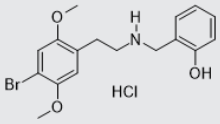
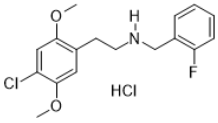
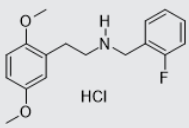
15510.20	N-Acetyl 25I-NBOMe (N-acetyl 2C-I-NBOMe)		2748301-01-9
11464.18	25N-NBOMe hydrochloride (2C-N-NBOMe HCl)		1566571-65-0
15444.20	C20-NBOMe hydrochloride (2,3-DMPEA-NB345OMe HCl; 2,3-DMPEA-NBTOMe HCl)		n/a
12108.19	N-MOB-5-APB hydrochloride hydrate (5-APB-NBOMe HCl H2O)		n/a

Closely related compounds

Chiron No.	Name	Structure	CAS
	NBF, NBOH and NBMD's		
14177.17	25B-NBOH hydrochloride (2C-B-NBOH HCl)		1539266-16-4
13067.17	25C-NBF hydrochloride (2C-C-NBF HCl)		1539266-21-1
10430.17	25C-NBOH hydrochloride (2C-C-NBOH HCl)		1539266-20-0

NBOMes product listing

ISO 17034
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Closely related compounds

Chiron No.	Name	Structure	CAS
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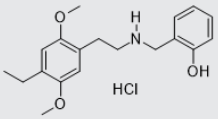
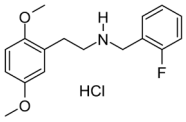
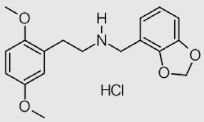
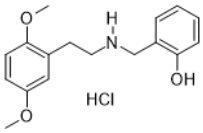
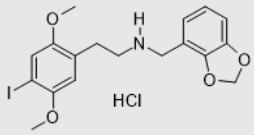
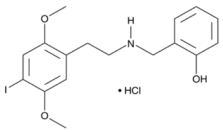
15792.19	25E-NBOH hydrochloride (2C-E-NBOH HCl)		1539266-40-4
11501.17	25H-NBF hydrochloride (2C-H-NBF HCl)		1177232-75-5 (free base)
11502.18	25H-NBMD hydrochloride (2C-H-NBMD HCl)		n/a
11496.17	25H-NBOH hydrochloride (2C-H-NBOH HCl)		919797-17-4 (free base)
11465.18	25I-NBMD hydrochloride (Cimbi-29)		1539266-14-2
11495.17	25I-NBOH hydrochloride (2C-I-NBOH HCl)		1539266-12-0

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