

\*This information was derived from drug materials experimentally and without analytical standard.  
This monograph was compiled in May 2026 and is subject to change.\*

## Compound Information

**Name:** Nefopam (Acupan)

**CAS Number:** 13669-70-0

**Chemical Formula:** C<sub>17</sub>H<sub>19</sub>NO

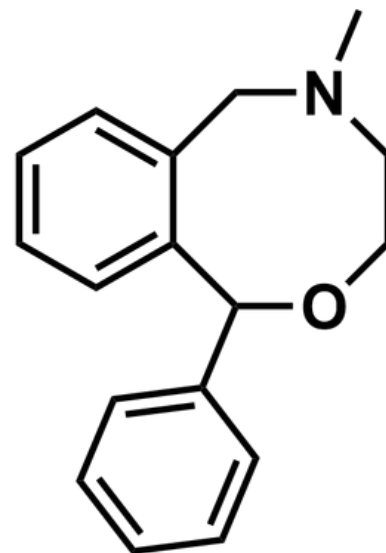
**IUPAC Name:** 5-methyl-1-phenyl-1,3,4,6-tetrahydro-2,5-benzoxazocine

**Molecular Weight:** 253.35

**Molecular Ion [M]<sup>+</sup>:** 253.1467

**Exact Mass [M+H]<sup>+</sup>:** 254.1540

First detection of Nefopam by Substance Drug Checking was made in February 2026 in white powder drug material received from a drug checking site in British Columbia. Compound detections to date have been made in samples expected to contain medetomidine, hydromorphone, cocaine, or unknown components.



Structure of Nefopam

**General:** Nefopam is a benzoxazocine compound investigated by Riker laboratories in the 1960s and 1970s as a diuretic and psychostimulant compound<sup>1</sup>. Nefopam has since been investigated as a non-opioid analgesic and used intermittently across Europe, Asia, and Oceania for treatment of neuropathic and post-operative pain. Other uses of Nefopam include the treatment of persistent hiccups as well as elimination of autonomic shivering. Nefopam was never market-authorized by Health Canada or the FDA.

**Mechanism:** Nefopam has a broad mechanism of action; targeting dopamine, serotonin, and dopamine monoamine re-uptake as well as having anticholinergic effects and speculated adrenergic agonism. Exploration of Nefopam for post-operative nociceptive analgesia show mixed results ranging from mild to moderate effect alone or in combination with NSAIDs and/or opioids.<sup>1,2</sup>

**Toxicity:** Nefopam overdose is characterized by fever, altered mental status and hallucinations, urinary retention, tachycardia, and hypotension. No reversal agents exist.

**Illicit Drug Supply:** The exact timeline upon which Nefopam entered the Canadian drug supply is unknown. It has persisted in the supply of fentanyl-containing samples and pressed pills across Canada with low to moderate prevalence since characterization in early 2026.

Like diphenhydramine (Benadryl), nefopam has been observed to produce erroneous positive result on BTNX fentanyl 2.0 strip tests. Dilution series has not been conducted at Substance to establish the threshold for cross-reactivity. There is literature mention of nefopam cross reactivity with benzodiazepine enzyme multiplied immunoassay; namely referencing homology with Oxazepam.<sup>3-5</sup>

## Literature

1. Bader, N. A.; Al-Ahmad, M. M.; Al Naeem, W.; Amer, M. G. Efficacy of nefopam in postoperative pain management: A systematic review of opioid consumption. *Journal of Applied Pharmaceutical Science* 2025, 15 (5) 24-39. doi: 10.7324/JAPS.2025.203223.

2. Jin, Y.; Myung, S.K.; Kang, H.; Eom, W.; Kim, D. Effects of intravenous nefopam on pain relief in patients with acute postoperative pain: A systematic review and meta-analysis of randomized controlled trials. *Korean Journal of Health Promotion* 2024, 24 (2) 56-66. doi: 10.15384/kjhp.2024.00052.

3. El-Haj, B.; Al-Amri, A.; Ali, H. Cross-reactivity of nefopam and its metabolites with benzodiazepine EMIT immunoassay. *Journal of Analytical Toxicology* 2008, 32 (9) 790-792. doi: 10.1093/jat/32.9.790.

4. Chavant, A.; Willeman, T.; Tonini, J.; Fonrose, X.; Boyer, J. C.; Cohen, S.; Guitton, J.; Stanke-Labesque, F. Cross-reactivity of nefopam and its metabolites on three different benzodiazepines immunoassay screenings: A comparative study. *Toxicologie Analytique et Clinique* 2020, 32 (4) 253-257. doi: 10.1016/j.toxac.2020.05.002.

5. Reid, K. Positive interference of the analgesic nefopam in the urine immunoassay for benzodiazepines in a secure setting. *Journal of Psychopharmacology* 2009, 23 (8) 997. doi: 10.1177/0269881108094298.

6. Dushna, O.; Dubenska, L.; Gawor, A.; Karasiński, J.; Barab, O.; Ostapiuk, Y.; Blazheyevskiy, M.; Bulska, E. Structural characterization and electrochemical studies of selected alkaloid N-oxides. *Molecules* 2024, 29, 2721. doi: 10.3390/molecules29122721.

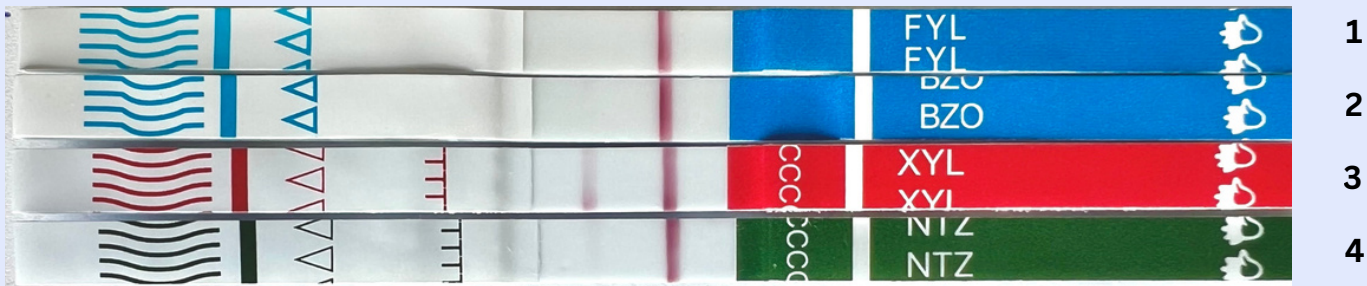
7. mzCloud: Advanced Mass Spectral Database. Thermo Fisher Scientific. <https://www.mzcloud.org> (Accessed July 3, 2026).

## Samples Containing Nefopam

| Expected Compound        | Description  | Detected Compound (s)           | FYL | BZO | MED | Date Received    | Location   |
|--------------------------|--------------|---------------------------------|-----|-----|-----|------------------|------------|
| Unknown                  | White powder | Nefopam                         | (+) | (+) | n/a | January 28, 2026 | Provincial |
| Unspecified "Painkiller" | White powder | Nefopam                         | (+) | (+) | n/a | March 10, 2026   | Envelope   |
| Cocaine                  | White powder | Nefopam, Caffeine               | (-) | n/a | n/a | March 13, 2026   | In-Person  |
| Hydromorphone            | White powder | Nefopam                         | (-) | (-) | n/a | March 17, 2026   | In-Person  |
| Hydromorphone            | White powder | Nefopam                         | (-) | (-) | n/a | March 17, 2026   | In-Person  |
| Medetomidine             | White powder | Nefopam                         | (+) | (+) | (+) | March 19, 2026   | In-Person  |
| Medetomidine             | White powder | Nefopam                         | (-) | (+) | (+) | March 19, 2026   | In-Person  |
| Medetomidine             | White powder | Nefopam, Fentanyl, Medetomidine | (+) | (+) | n/a | March 19, 2026   | In-Person  |
| Unknown                  | White powder | Nefopam                         | (+) | (+) | n/a | March 26, 2026   | Provincial |

FYL = fentanyl immunoassay test strip result, BZO = benzodiazepine immunoassay test strip result, MED = medetomidine immunoassay test strip result. Location represents if the sample was received from a provincial partner site, from an individual by mail, or in-person at our store front location in Victoria, BC.

## Lateral Flow Immunoassay Strip Tests

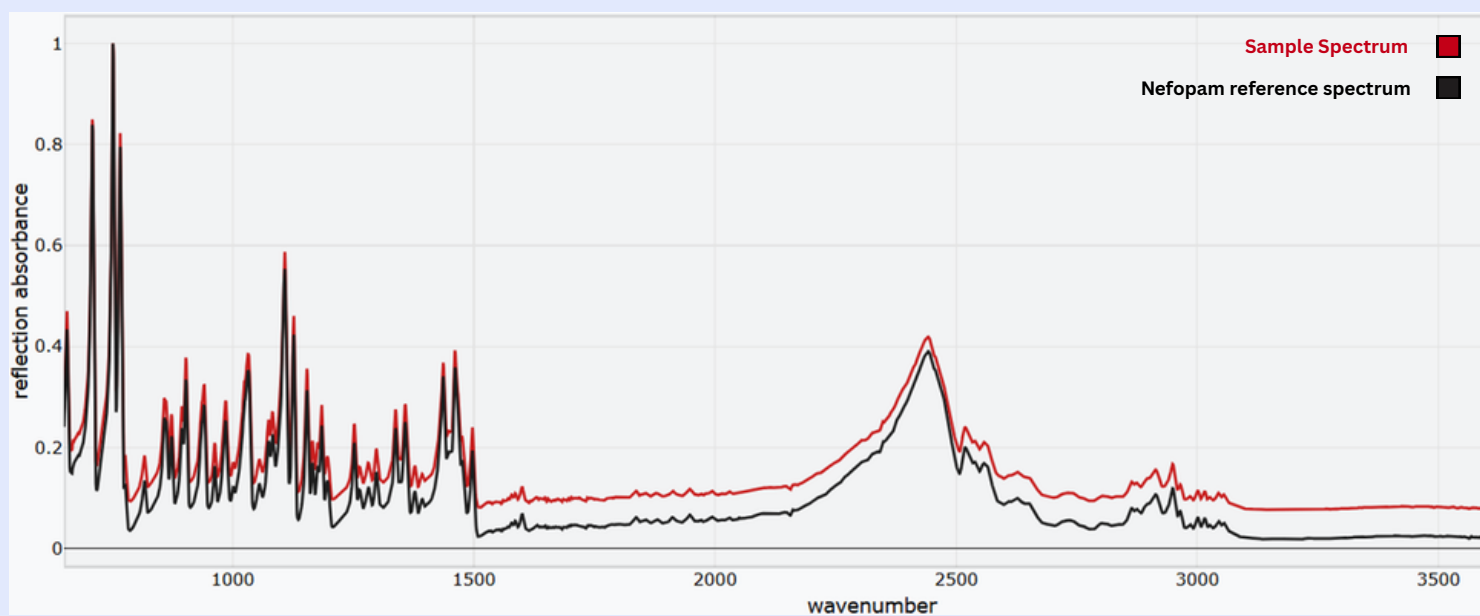
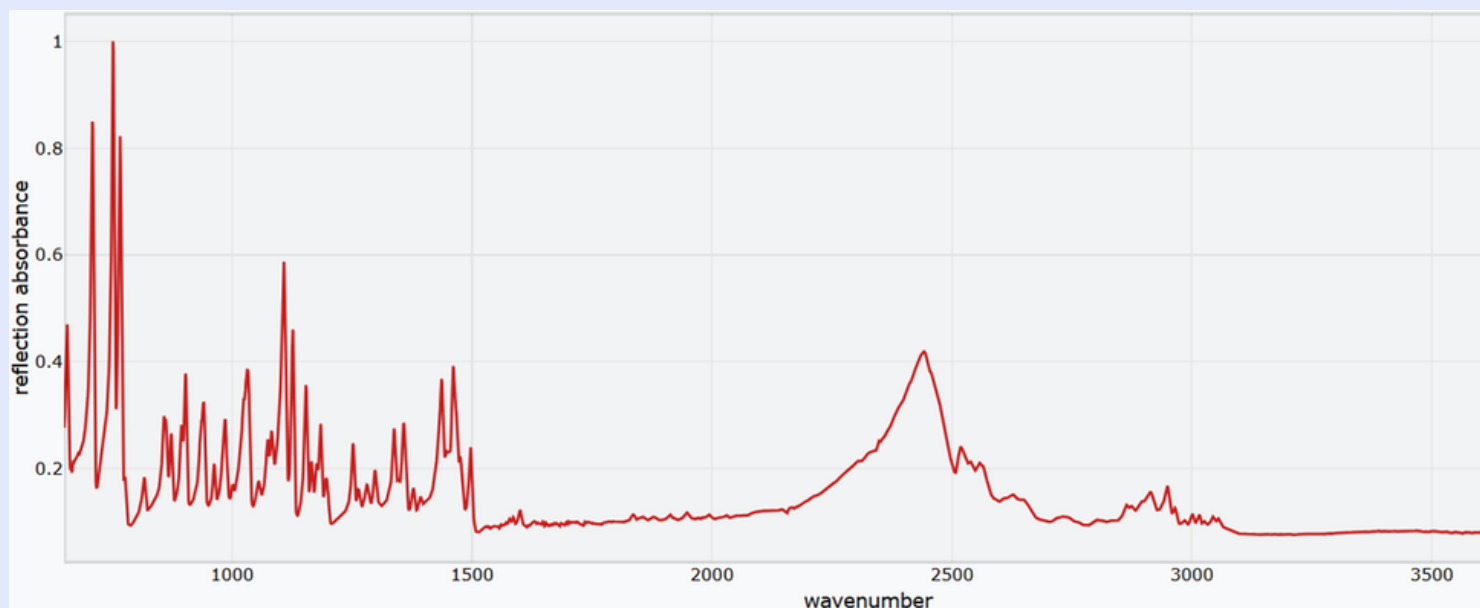


1. FYL-1S48; (20 ng/ml) | 2. BZO-1S3; (300ng/ml) | 3. XYL-18S2; (1000ng/ml) | 4. NTZ-18S26; (2000ng/ml)

## Methods

Immunoassay strip tests conducted in 1mg/ml sterile water at 38°C. Results were Interpreted after 5 minutes.

## FTIR

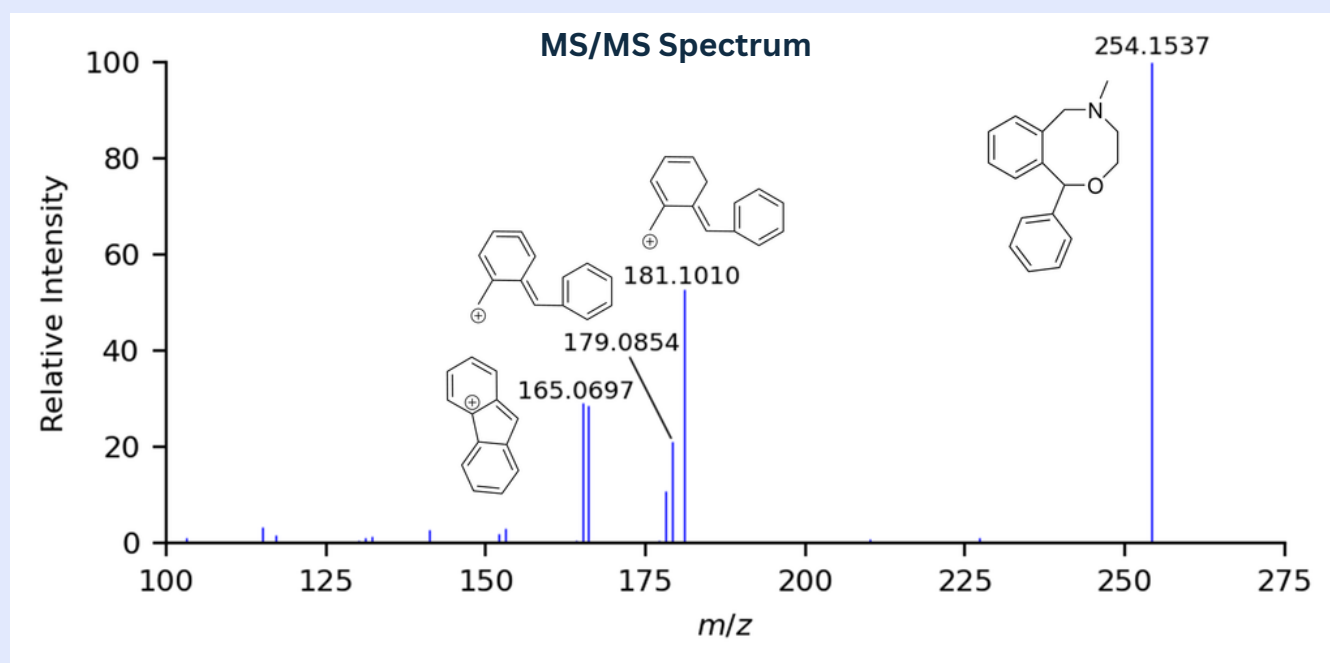
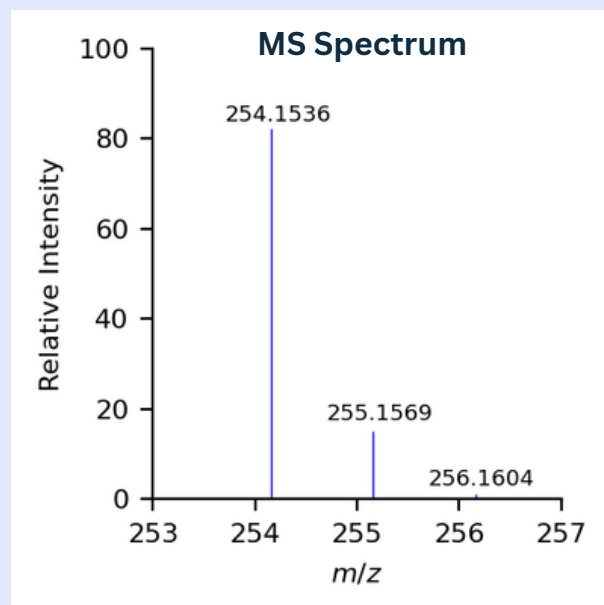
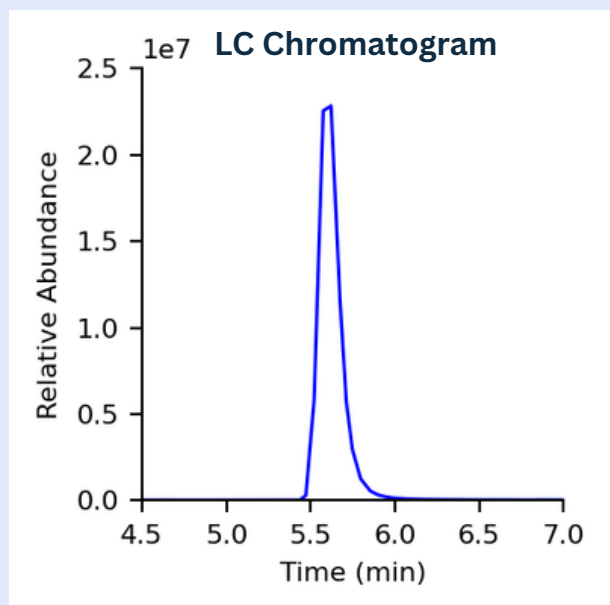


IR absorption scans of query compound (top figure) and query compound overlayed with the BCCSU library reference spectrum for nefopam (bottom figure).

## Methods

**Acquisition:** Agilent 4500a Series Portable FTIR with dTGS detector and single-bounce diamond ATR accessory. Spectral data was compiled over 32 scans in the 650-4000 ( $\text{cm}^{-1}$ ) range with a spectral resolution of 4( $\text{cm}^{-1}$ ) and zero fill factor of 4.

# Orbitrap LC - HRMS



LC chromatogram, LC-MS precursor ion spectrum, and LC-MS/MS spectrum. The MS/MS data was compared to previously reported fragmentation information for nefopam.<sup>6</sup> Structural annotation was informed by mzcloud<sup>7</sup> and Mass Frontier™ (Thermo Fisher Scientific, Waltham, MA, USA).

## Methods

**Instrument:** Orbitrap Exploris™ 120 with Thermo Scientific Vanquish™ HPLC

**Column:** Thermo Scientific Accucore™ aQ C18 polar endcapped column (100 x 2.1 mm, 2.6 µm pore size)

### Mobile Phase:

A: HPLC Grade Water + 0.1% Formic Acid

B: HPLC Grade Acetonitrile + 0.1% Formic Acid

Flow rate: 200 µL/min

**Gradient:** 0 min: 20% B, 3 min: 20% B, 13 min: 65% B, 14 min: 20% B, 15 min: End

### Temperatures:

Autosampler: 5 °C (sample storage temp)

Column Chamber and Precolumn

Chamber: 30 °C

ESI Source: 275 °C

### Targeted Acquisition Parameters:

1µL Injection

MS<sup>2</sup>: Precursor 254.2, 120 000 resolution

HCD: (5, 15, 20, 30, 50V)

DDMS<sup>2</sup>: Full Scan 150-750, 120 000 resolution