

Opioids in 28 dental plaque samples from patients undergoing long-term medication and comparison with samples from lethal intoxications

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Aims

Alternative matrices such as non-mineralized dental biofilm (plaque) can provide crucial information in post-mortem toxicology, but often data is scarce to interpret the results. Therefore, we aimed to gain information about drug concentration ranges in plaque samples from patients undergoing long-term medication. Plaque samples from patients in opioid replacement therapy (ORT) were investigated and the data were put into context with the drug results from post-mortem plaque samples in two lethal intoxications with methadone and morphine.

Methods

Clinical study

- 28 patients in ORT
- Study group 1: n=25
 - Methadone or Polamidon® (= levomethadone) syrup
 - 25 - 120 mg/d
- Study group 2: n=3
 - Substitol® capsules (= slow-release morphine)
 - 600 - 1,400 mg/d
- Plaque sampling ~24 h after the last and immediately before the next regular daily dose

Lethal intoxications

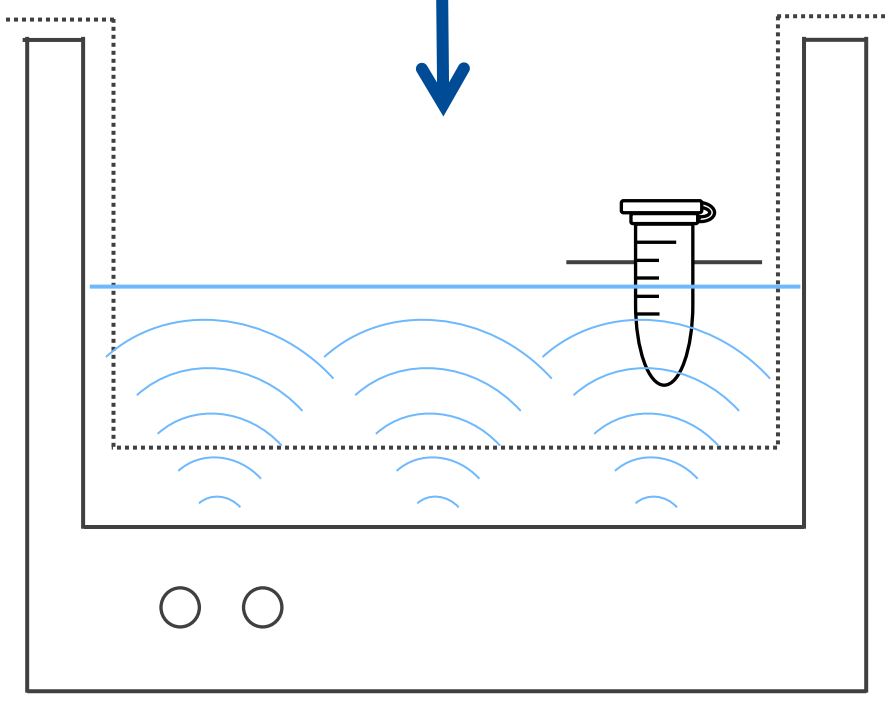
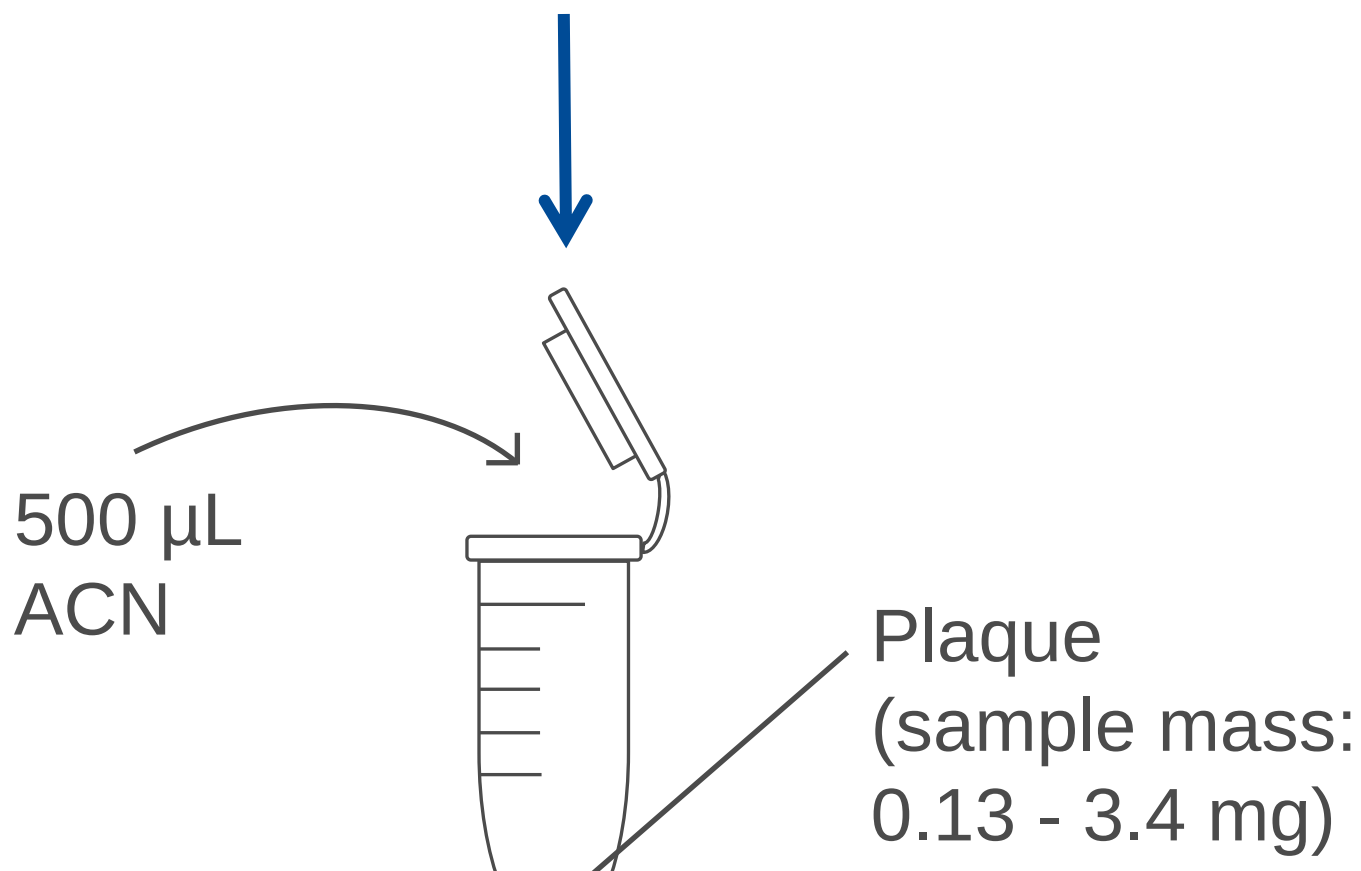
- Case 1: methadone+
- Case 2: morphine+
- Plaque sampling post-mortem

Sample Preparation

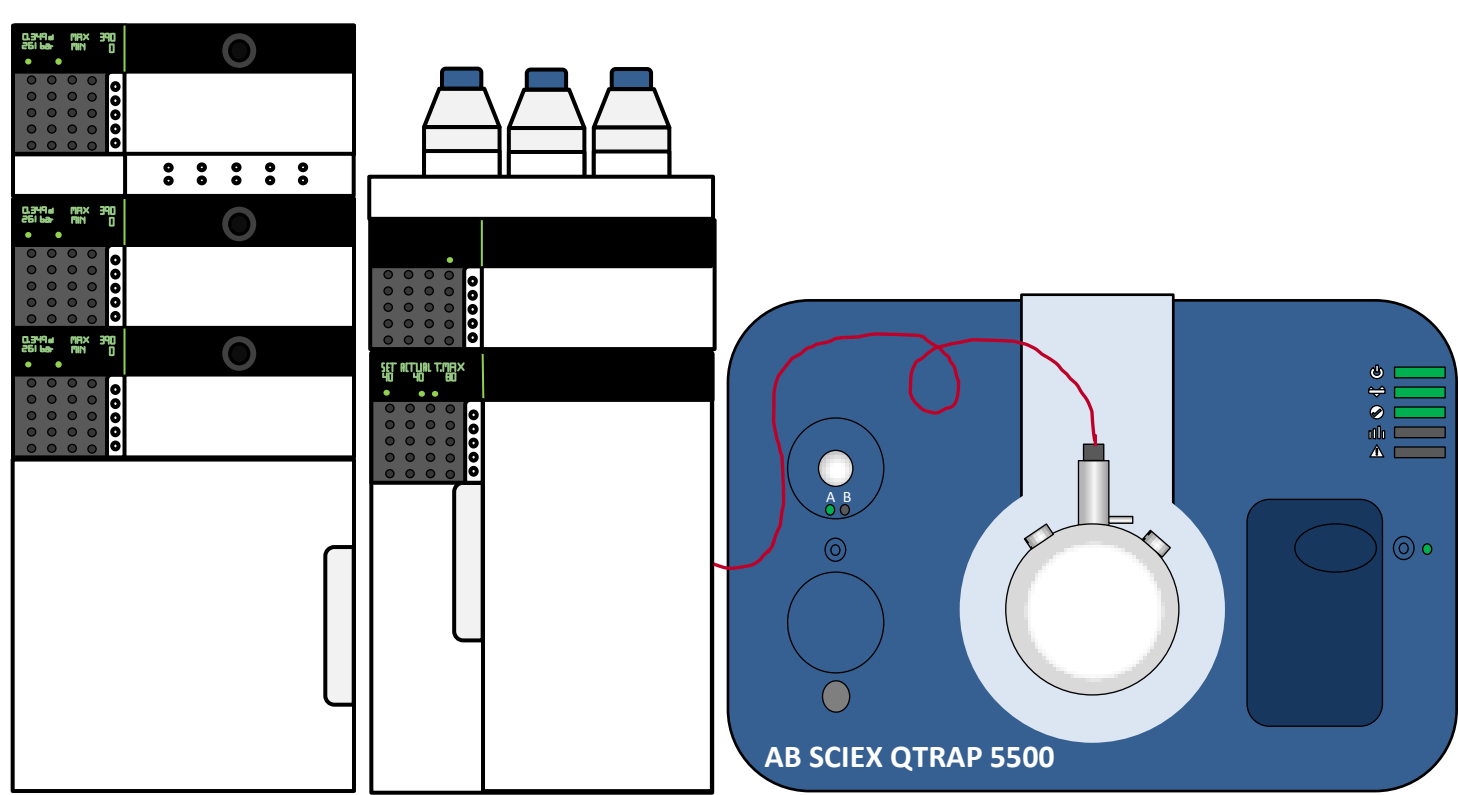


Dental scaler

Plaque sampling



10 min
ultrasonication



LC-MS/MS-Analysis^[1]

Results & Discussion – Clinical Study

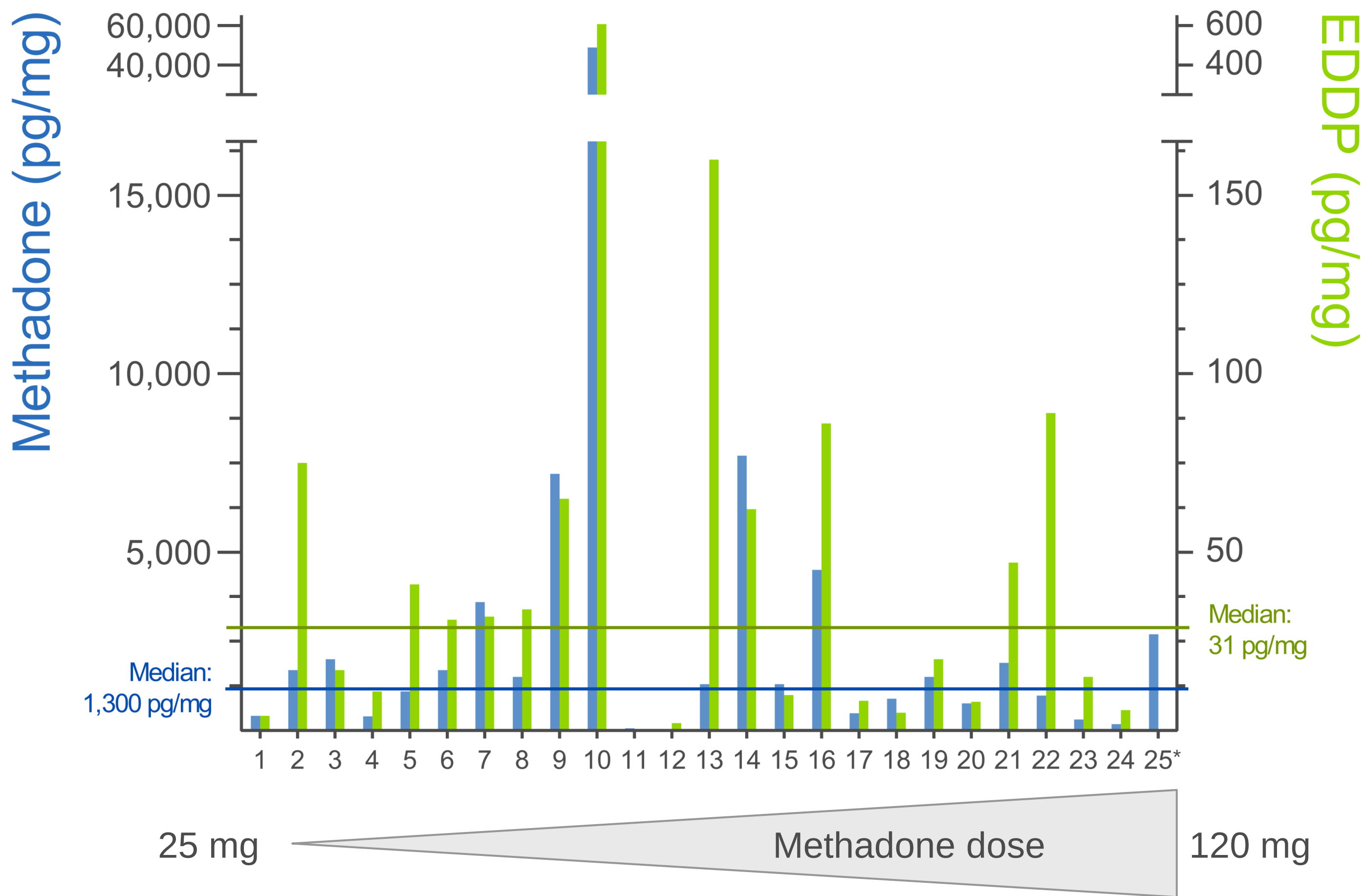


Fig. 1: Study group 1 – methadone and EDDP concentrations in plaque
*EDDP positive but not quantifiable

Study group 2	26	27	28
Dose [mg/d]	600	1,000	1,400
Morphine [pg/mg]	120 [#]	480 [#]	400
Normorphine [pg/mg]	n.d.	n.d.	n.d.

Tab. 1: Study group 2 – morphine and normorphine concentrations in plaque, n.d. = not detected

Study group 1:

- Wide concentration range:
 - Methadone: 42 - ~49,000 pg/mg
 - EDDP: ~2.1 - 610 pg/mg
- No correlation between daily dose and plaque concentration
- Compliance of the subjects?
 - Additional abusive uptake (e.g. patient 10?) or
 - “Drug holidays” = absence from the medical practice (e.g. patient 11 and 12?) ...should be considered

Study group 2:

- Morphine < methadone plaque concentration despite higher doses
 - Different modes of application (capsule vs. syrup)
- #Patient 26 and 27: additional findings of
 - 6-MAM (71 and ~110 pg/mg)
 - Codeine (57 and ~22 pg/mg) → Heroin co-use!
 - Biases plaque results: ...Higher morphine plaque concentrations than solely under long-term medication?

Median:
400 pg/mg

Results & Discussion – Lethal Intoxications

Case 1

- 31 ♀, in ORT with methadone
- Overdosed herself with methadone
- Dosage, mode of application and time of uptake unknown

Tab. 2: Case 1 – methadone and EDDP concentrations in blood and plaque

Case 1	Methadone	EDDP
Femoral blood [ng/mL]	6,700+	260
Plaque [pg/mg]	~110,000	1,900

80x↑

60x↑

...than median of study group 1, but time gap between drug uptake and death possibly < 24h

Case 2

- 86 ♀, suffered from Alzheimer’s disease
- Victim of an extended suicide by her husband
- Fatal oral morphine dose (liquid)
- Survived 1.5 days in hospital under naloxone therapy

Tab. 3: Case 2 – morphine and normorphine concentrations in blood and plaque

Case 2	Morphine	Normorphine
Femoral blood [ng/mL]	1,500 ⁺	not analyzed
Plaque [pg/mg]	~8,100	~52

20x↑

✓

...than median of study group 2, although different modes of application and heroin co-use in study group

Conclusions

The clinical study provides first data regarding plaque concentrations in patients under long-term medication with a special focus on opioids. High variances were observed, especially in study group 1. However, the presented data will help to interpret drug results in plaque, particularly in intoxication cases: Plaque concentrations in lethal intoxications are expected to be at least one order of magnitude higher than under therapeutic substance use, always keeping in mind possibly different settings of the cases (e.g. mode of application, time of uptake).

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Reference

[1] K. Henkel et al., Full validation of a method for the determination of drugs of abuse in non-mineralized dental biofilm using liquid chromatography-tandem mass spectrometry and application to postmortem samples, Talanta 176 (2018)