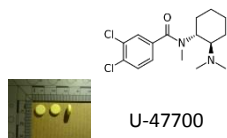


A case of U-47700 and flubromazepam intoxication: pharmacokinetic data

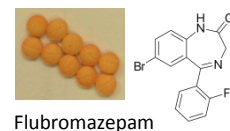
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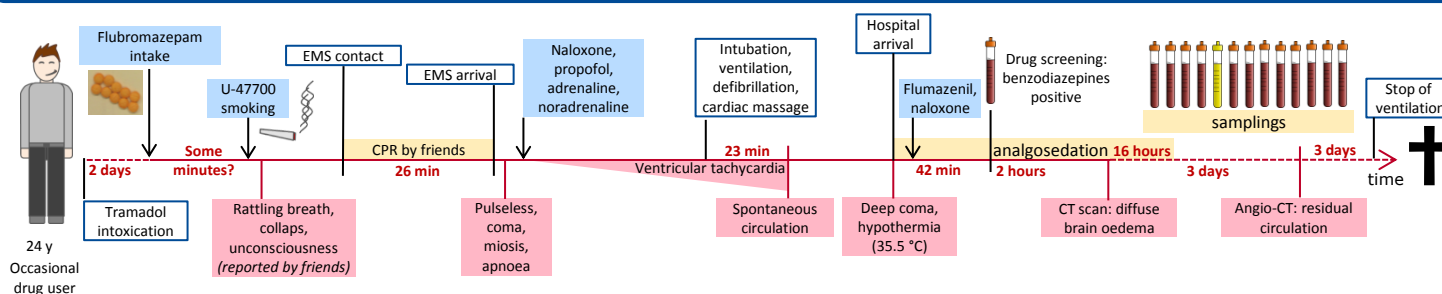
Background and Aim



Novel and highly potent synthetic opioids like U-47700 and designer benzodiazepines like flubromazepam are an **emerging trend** on the recreational drug market. Severe poisonings have been reported after consumption of U-47700 but still little is known about its pharmacokinetics. The aim of this study was to **report clinical symptoms and pharmacokinetic data** to support toxicologists and clinicians dealing with intoxications by new psychoactive substances.

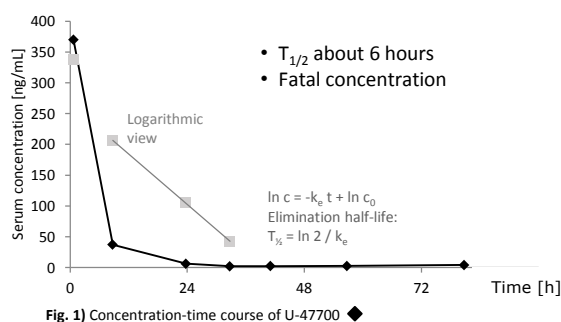


Case Report



Results

U-47700

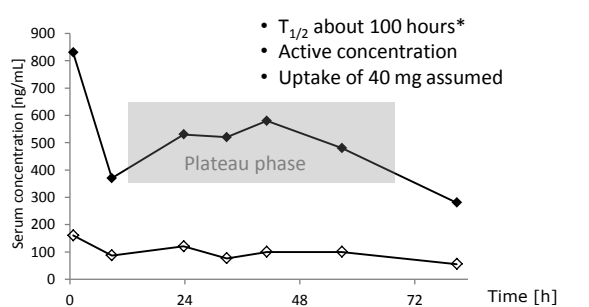


Toxicological and clinical values

| time since hospital admission [h] | U-47700 [ng/mL] | flubromazepam [ng/mL] | hydroxy-flubromazepam [ng/mL] | pregabalin [µg/mL] | creatinine [mg/dL] | urea nitrogen [mg/dL] | lactate [mmol/L] | ALAT [U/L] | ASAT [U/L] | INR | PTT [s] | CRP [mg/dL] |
|-----------------------------------|-----------------|-----------------------|-------------------------------|--------------------|--------------------|-----------------------|------------------|------------|------------|-------|---------|-------------|
| 42 min | 370 | 830 | 160 | 1.7 | 1.47 | 9 | 5.06 | 360 | 339 | 0.99 | 35.2 | 1.15 |
| 9 | 37 | 370 | 87 | 1.3 | 1.10 | 11 | 1.44 | 295 | 256 | 1.02 | 36.2 | 1.7 |
| 24 | 6.3 | 530 | 120 | 0.29 | 1.07 | 9 | 1.91 | | | 1.06 | 40.6 | 7.82 |
| 33 | 2.1 | 520 | 76 | 0.24 | 1.30 | 8 | 2.90 | 164 | 97 | 1.12 | 40.1 | 12.1 |
| 41 | 2.3 | 580 | 100 | ≈0.12 | | | 2.54 | | | | | |
| Urine 41 | 2 | 13 | 310 | 1.39 | < 13 | | | | | | | |
| 48 | | | | | 1.06 | 5 | 2.05 | 135 | 104 | 1.44 | 52.1 | 15.6 |
| 57 | 2.6 | 480 | 100 | ≈0.062 | 1.08 | 5 | 1.38 | | | 1.28 | 56.2 | 18.5 |
| 64 | | | | | 1.10 | 6 | 1.17 | 112 | 202 | 1.18 | 50.4 | 20.3 |
| 72 | | | | | 1.15 | 8 | 1.08 | 109 | 261 | 1.09 | 48.7 | 24.2 |
| 81 | 4.2 | 280 | 55 | ≈0.062 | 1.24 | 11 | 1.29 | 84 | | 1.06 | 50.4 | 25.3 |
| 96 | | | | | 1.14 | 13 | 1.20 | | 362 | 0.99 | 46.5 | 27.2 |
| 105 | | | | | | 14 | 0.82 | | 341 | 1.00 | 47.1 | 25 |
| 129 | | | | | | 16 | 0.79 | | | 1.01 | 46.3 | 15.4 |
| reference range | | | | | 0.6-1.3 | 10-22 | 0.5-1.6 | < 45 | < 35 | < 1.3 | 25-38 | < 0.8 |

¹⁾ Laboratory values also remarkable in this blood serum sample: troponin 0.42 ng/mL (reference range < 0.04 ng/mL), CK 304 U/L (reference range < 170 U/L), CKMB 101 U/L (reference range < 26 U/L) and LDH 375 U/L (reference range 120 – 240 U/L)

Flubromazepam



* Comparable to Moosmann B et al. J Mass Spectrom. 2013;48:1150-1159.

Discussion

- U-47700 half life is comparable to morphine.
- Due to a 7.5 higher antinociceptive activity than morphine, the U-47700 concentration can be stated as fatal.
- Careless consumption of U-47700 might be triggered by cognitive impairment by flubromazepam.

Methods

- LC-QToF-MS screening of urine after acetonitrile precipitation (Bruker maXis impact II QToF)
- LC-MS/MS (Sciex API5000)
- Opioids: 100 µL sample, automated SPE
- Benzodiazepines: 100 µL, alkaline LLE
- LOQ U-47700: 1.0 ng/mL
- LOQ Flubromazepam: 0.8 ng/mL

Conclusion

The extremely long elimination half-life of flubromazepam may lead to **prolonged central-nervous depressant effects** which may be unexpected and should be considered by drug consumers as well as clinicians at emergency departments. In the presented case, **synergistic respiratory depression** as a consequence of the combined intoxication by the synthetic opioid U-47700 and flubromazepam can be stated as the cause of death.

Literature

K. Koch, V. Auwärter, M. Hermanns-Clausen, M. Wilde, M. A. Neukamm: Mixed intoxication by the synthetic opioid U-47700 and the benzodiazepine flubromazepam with lethal outcome: Pharmacokinetic data, *Drug Testing and Analysis* 2018, 10 (8), 1336-1341

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