

# Abuse of the synthetic opioid U-47700 in military conflicts

## Abus de l'opioïde synthétique U-47700 dans les conflits militaires

J. Patočka <sup>1,2</sup>, V. Gajdošík <sup>3</sup>, R. Jelínková <sup>4</sup>, M. Malík <sup>5</sup>, Z. Navrátilová <sup>6</sup>. CZECH REPUBLIC

### Summary

In recent years, U-47700 has come into the spotlight for its illegal abuse, particularly in Western countries, where it has been sold as a heroin substitute or mixed with other opioids such as fentanyl. Due to its high potency and risk of addiction and overdose, U-47700 has been placed on the banned substance list in many countries. In the context of war conflicts, it is of particular concern that this powerful opioid can be misused for several illegitimate purposes. It can be abused in field conditions as a pain reliever for wounded warriors. With its power, it can temporarily allow the injured to continue fighting, even if it means the risk of addiction or overdose. In some conflicts, drugs like U-47700 may be used to manipulate and control combatants or the civilian population. The illegal production and distribution of drugs like U-47700 can further destabilize conflict-affected areas, as revenue from drug sales can finance further violence and terrorism.

**Key words:** U-47700, synthetic opioid, abuse, military conflicts.

### Résumé

Ces dernières années, l'U-47700 a été mis sous le feu des projecteurs en raison de son abus illégal, notamment dans les pays occidentaux, où il a été vendu comme substitut à l'héroïne ou mélangé à d'autres opioïdes comme le fentanyl. En raison de sa puissance élevée et de son risque de dépendance et de surdosage, l'U-47700 a été inscrit sur la liste des substances interdites dans de nombreux pays. Dans le contexte des conflits de guerre, il est particulièrement préoccupant que ce puissant opioïde puisse être utilisé à mauvais escient à plusieurs fins illégitimes. On peut en abuser sur le terrain comme analgésique pour les guerriers blessés. Grâce à sa puissance, il peut permettre temporairement aux blessés de continuer à se battre, quitte à risquer une addiction ou une surdose. Dans certains conflits, des drogues comme l'U-47700 peuvent être utilisées pour manipuler et contrôler les combattants ou la population civile. La production et la distribution illégales de drogues comme l'U-47700 peuvent déstabiliser davantage les zones touchées par le conflit, dans la mesure où les revenus issus de la vente de drogues peuvent financer davantage de violence et de terrorisme.

**Mots clés:** U-47700, l'opioïde synthétique, abus, les conflits militaires.

### Introduction

U-47700 is a synthetic opioid with a high risk of addiction and overdose. The drug was originally developed in the 1970s by the pharmaceutical company Upjohn as a potential pain reliever, but was never approved for medical use. Nevertheless, in

recent years it has started to be produced and distributed illegally, especially on the black market [1]. The drug has earned the nickname "pink heroin" because of its appearance and effects, which are often described as similar to heroin, even though it is chemically different. Due to the high risk associated with its use, it has been placed on the list of prohibited substances in many countries, including the United States.

### Synthetic opioids

Synthetic opioids are one of a group of new psychoactive substances (NPS) that has seen an alarming increase in use worldwide in recent years. The main reason is their easy availability on the Internet, the price, and last but not least, the fact that they are not provable using standard drug tests. This represents a significant health and social problem. NPS are chemical compounds that have been designed to simulate the effects of known drugs such as marijuana, cocaine, or ecstasy. These substances are

often created by slight modifications of existing chemical structures to make them difficult to detect with conventional drug tests and to circumvent legal restrictions [2].

### NPS risks

The increase in the use of NPS brings a number of risks, the first of which are health risks. Many NPS have not been properly studied for their effects on the human organism [3]. Their uncontrolled use can lead to adverse health effects such as poisoning, heart problems, psychological disorders and even death. A significant problem is the fact that many NPS are addictive and cause serious psychological problems. Another risk is legal issues: Due to the rapidly changing nature of NPS, there may be problems with the classification and regulation of these substances [4]. Many countries are trying to update their laws to include new substances, but this is difficult due to the speed with which new sub-

1. Faculty of Health and Social Studies, Institute of Radiology, Toxicology and Civil Protection, University of South Bohemia Ceske Budejovice, 37005, Ceske Budejovice, Czech Republic

2. Department of Chemistry, Faculty of Science, University of Hradec Kralove, 50003, Hradec Kralove, Czech Republic

3. St. Elizabeth College of Health and Social Work in Bratislava, 811 02 Bratislava, Slovakia

4. NBC Defence Institute, University of Defence, 66210, Brno, Czech Republic

5. Department of Agroenvironmental Chemistry and Plant Nutrition, Faculty of Agrobio-logy, Food and Natural Resources, Czech University of Life Sciences Prague, 165 00 Praha, Czech Republic

6. Department of Botany, Faculty of Science, Charles University, 128 00 Praha, Czech Republic

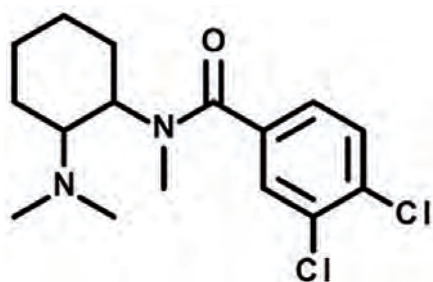
stances appear [5]. Their illegal production and trafficking has a major impact on crime and the illegal economy [6,7]. Lack of information is also a serious risk. Users of NPS often lack information about the effects, dosage and risks of these substances. This increases the likelihood of dangerous situations [8]. To get an idea of the danger that NPS drugs pose to society, let's say that estimates of drug overdose deaths in the US alone exceeded 60,000 people already in 2016 [9] and since then they are still growing.

## NPS protection

The fight against the increase in NPS use is very complex. Indeed, it includes cooperation between health and legal institutions, educational programs for the public and users, strengthening of border controls and monitoring of new substances [10]. One such dangerous NPS is the substance code-named U-47700, also commonly known as U4 or pink heroin, to which this article is dedicated [11]. It came to the attention of "non-pharmaceutical" users when it began to be offered as a "research chemical" on Internet forums and in illegal online trade as a drug with opioid effects. It has quickly become a very popular recreational drug that brings serious health problems, including overdose and death. Many reports of deaths related to U-47700 have led to its ban and regulation in many countries, but the numbers of its users tend to increase [12]. It is important to remember that the use of illegal drugs, especially those that have not been scientifically researched and approved, is very dangerous. These substances do not have a standardized quality or dosage, which increases the risk of serious health consequences.

## Chemistry and Pharmacology U-47700

The U-47700 molecule is composed of a benzamide nucleus substituted at positions 3 and 4 by chlorine atoms, and a cyclohexyl ring is attached to the amide



nitrogen, which is substituted by a dimethylamino group at the second position. The systematic name of U-47700 is 3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide [11].

U-47700 acts as a selective agonist at the  $\mu$ -opioid receptor, the same receptor that other opioids such as morphine and heroin also target. Activation of these receptors leads to pain relief, euphoria and sedation. As previously mentioned, U-47700 is significantly more potent than morphine [13,14]. This high potency increases the risk of overdose, especially when taken in amounts similar to less potent opioids.

## Metabolism and Excretion

U-47700 is metabolized in the liver, where it undergoes N-demethylation and O-demethylation. Metabolites and the parent compound are then excreted by the kidneys [15].

## Adverse effects, Risks and Toxicity

Common side effects associated with opioid use, such as drowsiness, constipation, and nausea, are also present with U-47700. However, the risk of severe respiratory depression is much higher. Due to its high potency, even small doses of U-47700 can lead to an overdose. Symptoms of overdose include severe respiratory depression, unconsciousness, and potentially death if not treated immediately with naloxone [16,17].

## The use of U-47700 in wartime conflicts

War conflicts often create an environment where drugs are abused, both by civilians and soldiers. Synthetic opioids such as U-47700 can be abused in war zones for several reasons:

**Pain relief:** In combat zones, access to medical care is often limited and injuries must be treated in field conditions. U-47700 and similar substances can be abused as a pain reliever, especially in situations where legal drugs are not available.

**Psychological relief:** Soldiers and civilians alike may abuse opioids to escape the stress, trauma, and horrors of war. Drugs can provide temporary relief from anxiety, fear, and other negative emotions associated with conflict.

**Drug trade:** In unstable regions where there are armed conflicts, the distribution of drugs such as U-47700 can be a form of fi-

ancing for various armed groups. Drugs can be smuggled and sold to finance military operations or support local economies decimated by war.

**Military use:** In some cases, opioids may also be used by soldiers to maintain alertness, overcome fear, or enhance performance. Although the use of U-47700 in this context is not well documented, other drugs have been similarly abused in military conflicts in the past.

Abuse of U-47700 in war zones carries many risks, including overdose, addiction, and health deterioration. An overdose of U-47700 is particularly dangerous because the drug is much stronger than traditional opioids such as morphine and can therefore easily lead to death, especially if medical attention is not provided. The abuse of synthetic opioids in war zones can also contribute to destabilizing regions, financing terrorist activities and prolonging conflicts. Given these facts, it is important to monitor and respond to the misuse of substances such as U-47700 not only in a civilian but also in a military context in order to minimize their harm and impact on human lives and regional stability. Like other opioids, U-47700 has a high potential for abuse and addiction. Repeated use can lead to physical dependence and withdrawal symptoms after discontinuation.

## Legal status

In recent years, as U-47700 has become popular in the illegal market due to its strong analgesic power, which is comparable to heroin or fentanyl, and due to its danger and risk of overdose, the synthetic opioid U-47700 has been gradually banned in various countries around the world. In 2016, the US Drug Enforcement Administration (DEA) listed U-47700 as a controlled substance, specifically Schedule I, meaning it is considered a substance with a high potential for abuse and no recognized medical use. In the European Union, U-47700 was placed on the list of controlled substances in 2018, which means that its production, distribution and sale are prohibited in all EU member states. In Canada, U-47700 is listed as a controlled substance and is illegal to manufacture, sell or possess without a permit. Also in Australia and New Zealand, the drug is classified as an illegal drug and it is prohibited to manufacture, distribute or possess it. In Russia, U-47700 is also classified as a prohibited substance, and China has classified it as a controlled

substance, and its production and distribution are illegal.

## Detection of substance U-47700

With the growth of the market for recreational illegal drugs, there is an increase in the occurrence of synthetic opioids, including the substance denoted by the abbreviation U-47700. Therefore, a number of analytical methods have been developed to determine these substances in the body of drug overdose victims. For the analysis of urine or blood samples, for example, a method using the instrumentation liquid chromatograph coupled to a triple quadrupole tandem mass spectrometer (LC-MS/MS) with a detection limit of 0.5 ng.ml<sup>-1</sup> is used. When checking the blood, the amount of the substance U-47700 in the range of 17-490 ng.ml<sup>-1</sup> was found in the forensic analysis of several overdosed persons [18]. LC-MS/MS and LC-QTOF methods are also used to determine the values of this particular substance, as well as other synthetic opioids such as *N*-ethylhexedrone, adinazolam, 4-chloromethcathinone or fentanyl derivatives, in biological materials [19]. In the autopsy samples of the case of fatal intoxication, the substance U-47700 was detected and quantified by ultra-high-performance liquid chromatography-tandem mass spectrometry (UH-PLC-MS/MS); the concentration of the substance in the blood reached a value of 1,470 ng.ml<sup>-1</sup> [20]. In other cases, quantification of U-47700 in blood samples was performed using the SPE/LC-ESI-MS/MS method, which demonstrated a range of substance concentrations of 83-24,000 ng.ml<sup>-1</sup> [21]. Some recent studies, with the help of sophisticated technical methods, deal with the question of whether the substance U-47700 can contribute, for example, to time-dependent postmortem redistribution in the organism [22]. The results of the study can contribute to a more accurate analysis of the presence of the substance in biological materials.

## Conclusion

U-47700, also known as "pink" or "U4", is a dangerous synthetic opioid with no legitimate medical use, primarily associated with high overdose potential and significant health risks. It is now controlled in many countries due to its potential for harm. Due to the speed with which new synthetic drugs appear on the market and interna-

tional regulatory changes, the legal status of U-47700 may change. However, most developed countries have already banned or heavily regulated this drug. In some conflicts, particularly where access to traditional opioids is limited, synthetic drugs such as U-47700 may be used as combat drugs. These substances can temporarily increase fighters' resistance to pain and fatigue, which can lead to dangerous and aggressive behavior. Historically, similar substances, such as amphetamines, have been used in military conflicts to maintain alertness and reduce feelings of hunger or exhaustion. Drug trafficking, including synthetic opioids, often serves as a source of funding for various armed groups and terrorist organizations. Drugs like U-47700 can be produced relatively cheaply and sold at a high profit on the black market, making it possible to obtain funds for the purchase of weapons and other equipment. Synthetic opioids such as U-47700 pose a serious threat not only to public health, but also to security in areas where they are used in the context of war and conflict.

## Literature

1. Rohrig TP, Miller SA, Baird T. R. U-47700: a not so new opioid. *JAT*. 2018;42(1):e12-e14.
2. Elliott S, Evans J. A 3-year review of new psychoactive substances in casework. *Forensic Sci Int*. 2014;243:55-60.
3. Reuter P. Options for regulating new psychoactive drugs: a review of recent experiences.

- London: UK Drug Policy Commission (UKDPC) 2011.
4. Stevens A, Measham F. The 'drug policy ratchet': Why do sanctions for new psychoactive drugs typically only go up? *Addiction*. 2014;109(8):1226-1232.
  5. Reuter P, Pardo B. Can new psychoactive substances be regulated effectively? An assessment of the British Psychoactive Substances Bill. *Addiction*. 2017;112(1):25-31.
  6. Sinha R, Easton C. Substance abuse and criminality. *JAAPL*. 1999;27(4):513-526.
  7. Sumnall HR, Evans-Brown M, McVeigh J. Social, policy, and public health perspectives on new psychoactive substances. *DTA*. 2011;3(7-8):515-523.
  8. Vári V. Crimes related to new psychoactive substances in rural segregates of Miskolc in Hungary. *BELÜGYI SZAKMAI TUDOMÁNYOS FOLYÓIRATA* (2010-). 2020;70(Spec.):37-57.
  9. O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths involving fentanyl, fentanyl analogs, and U-47700—10 states, July–December 2016. *MMWR*. 2017;66(43):1197.
  10. Baumann MH, Volkow ND. Abuse of new psychoactive substances: threats and solutions. *Neuropsychopharmacol*. 2016;41(3):663-665.
  11. Baumann MH, Tocco G, Papsun DM, Mohr AL, Fogarty MF, Krotulski AJ. U-47700 and its analogs: non-fentanyl synthetic opioids impacting the recreational drug market. *Brain Sci*. 2020;10(11):895.
  12. Darke S, Peacock A, Duflou J, Farrell M, Lappin J. Characteristics of fatal 'novel' synthetic opioid toxicity in Australia. *Drug Alcohol Depend*. 2022;232: 109292.
  13. Nikolaou P, Katselou M, Papoutsis I, Spiliopoulou C, Athanaselis, S. U-47700. An old opioid becomes a recent danger. *Forensic Toxicol*. 2017;35:11-19.
  14. Park H, Lin M, Zhou L, Eubanks LM, Zhou B,

## PROF. RNDr. Jiří PATOČKA, DrSc.



Jiří Patočka, born April 24, 1939 in Veverská Bítýška, Brno-venkov district, Czech Republic, is a Czech toxicologist and university teacher. He graduated from the Faculty of Natural Sciences of the Masaryk University in Brno. He obtained the title of Candidate of Chemical Sciences at the Institute of Organic Chemistry and Biochemistry of the Czechoslovak Academy of Sciences in Prague. He worked as a scientific researcher and teacher at the Military Medical Academy in Hradec Králové and at the University of South Bohemia

in České Budějovice. He currently works as an external employee of the Health and Social Sciences Faculty of the University of South Bohemia in České Budějovice and the Faculty of Science of the University of Hradec Králové. He is an emeritus Professor at the Faculty of Military Health at the University of Defense in Hradec Králové. He is a member of several professional societies and a member of the editorial board of two scientific journals (Military Medical Science Letters and the Journal of Applied Biomedicine, of which he is a co-founder).

Professor Patočka is the author or co-author of a number of scripts and textbooks (e.g. Military toxicology, Grada publishing house 2004), author of chapters in 8 monographs and together with Prof. Struneckou is the author of five popular scientific books published in the Czech Republic and Slovakia. He gave more than 80 lectures at home and abroad and was the principal investigator of 3 grant research tasks. His scientific career is characterized by 661 professional articles in scientific journals, 8510 citations. Hirsch index = 42 and i10-index = 135. Operates the TOXICOLOGY server (<https://www.toxicology.cz>).

- Janda KD. Development of a vaccine against the synthetic opioid U-47700. *Front Pharmacol.* 2023;14:1219985.
15. Krotulski AJ, Mohr AL, Papsun DM, Logan BK. Metabolism of novel opioid agonists U-47700 and U-49900 using human liver microsomes with confirmation in authentic urine specimens from drug users. *DTA.* 2018;10(1):127-136.
  16. Ruan X, Chiravuri S, Kaye AD. Comparing fatal cases involving U-47700. *Forensic Sci Med Pathol.* 2016;12:369-371.
  17. Rambaran KA, Fleming SW, An J, Burkhardt S, Furmaga J, Kleinschmidt KC, Spiekerman AM, Alzghari SK. U-47700: a clinical review of the literature. *J Emerg Med.* 2017;53(4):509-519.
  18. Mohr LA, Friscia M, Papsun D, Kacinko SL, Buzby D, Logan BK. Analysis of Novel Synthetic Opioids U-47700, U-50488 and Furanyl Fentanyl by LC-MS/MS in Postmortem Casework. *JAT.* 2016;40:709-717.
  19. Fleming SW, Cooley JC, Johnson L, Frazee CC, Domanski K, Kleinschmidt K, Garg U. Analysis of U-47700, a Novel Synthetic Opioid, in Human Urine by LC-MS-MS and LC-QToF. *JAT.* 2017;41:173-180.
  20. Nowak K, Szpot P, Zawadzki M. Fatal intoxication with U-47700 in combination with other NPS (N-ethylhexedrone, adinazolam, 4-CIC, 4-CMC) confirmed by identification and quantification in autopsy specimens and evidences. *Forensic Toxicology.* 2021;39:493-505.
  21. Rojek S, Romańczuk A, Kula K, Synowiec K, Kłys M. Quantification of U-47700 and its metabolites: *N*-desmethyl-U-47700 and *N,N*-didesmethyl-U-47700 in 12 autopsy blood samples employing SPE/LC-ESI-MS-MS. *Forensic Toxicol.* 2019;37:339-349.
  22. Nordmeier F, Doerr AA, Potente S, Walle N, Laschke MW, Menger MD, Schmidt PH, Meyer MR, Schaefer N. Are the (New) Synthetic Opioids U-47700, Tramadol and Their Main Metabolites Prone to Time-Dependent Postmortem Redistribution?—A Systematic Study Using an In Vivo Pig Model. *JAT.* 2023;47:236-244.

## 13th MME Course 2025 (hybrid)

The International Committee of Military Medicine, the ICMM Reference Centre for Education of International Humanitarian Law and Ethics, and the Swiss Armed Forces Medical Services Directorate offer a course on **Military Medical Ethics (MME)** to Military Medical Personnel, Military Medico-Legal Officers, and Chaplains as well as other interested members of the armed forces.

**14-19.09.2025**

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### General Information on the Military Medical Ethics Course

This **advanced course** aims at qualifying the participants to make correct decisions in situations where competences in international law and ethics are similarly relevant. The capacity is built and trained by means of **case studies which are drawn on situations and reports from recent deployment**.

The concrete cases and topics can vary from year to year and will reflect current needs. **Cases from the experience of course participants are welcome** but should be made in advance to allow for a sound preparation of the analysis

### The course aims to

- Enable participants to recognise and **analyse situations that present ethical and legal dilemmas** in contemporary military operations.
- Equip participants with the **tools to make legally and ethically sound decisions** in situations where **competencies in international law and ethics** are equally relevant.

### Course Program

- The provisional **Course program** can be downloaded on the website : <https://www.melac.ch/courses-workshops/ethics-courses/mme-hybrid-2025> Information about the mandatory e-learning before the course further below on this page!
- All participants must complete the **preparatory e-learning** and some assignments before the main course in weeks 35-37 (starting August 25, 2025). A total of 5-7 hours will be required to complete the e-learning.
- For **questions** regarding the course or the registration, please contact [mme-loac.lba@vtg.admin.ch](mailto:mme-loac.lba@vtg.admin.ch)

### Hybrid Classroom Course 2025

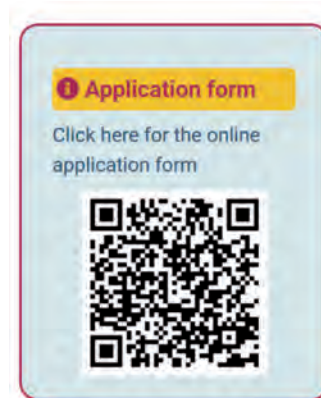
The 13th ICMM Course on Military Medical Ethics in Times of Armed Conflict (Military Medical Ethics/ MME) will be held as a

hybrid classroom course with participants both on-site in Schwarzenberg LU, Switzerland and online.

In **preparation for the course**, participants will get access to an **e-learning tool** and will have to follow some exercises online. Participants are free to schedule when they do these tasks (which amount to about 5-7h in total) within three weeks before the course.

The **main course will be held on-site and via videoconferencing** and the participants and teachers will meet during **fixed times in the virtual environment**. Hence, the usual format of the course that includes some lectures and much groupwork and discussions will be transferred into a hybrid classroom. In addition, external experts may join the course for lectures. Thus, the hybrid course shall be as close to the onsite course format as possible and shall offer as much direct exchange between the participants and the teaching team as possible.

### Application for the course



For **questions** regarding the course or the registration, please contact [mme-loac.lba@vtg.admin.ch](mailto:mme-loac.lba@vtg.admin.ch)

**For more information on costs, ...please visit the website :** <https://www.melac.ch/courses-workshops/ethics-courses/mme-hybrid-2025>

### Language

- The course is held in **English language**. Participants must have sufficient knowledge in English to read texts, understand presentations, and to participate in discussions.