



## CRACKING DOWN ON DRUG ABUSE: OPIOID-FREE C-SECTIONS REPORT #2737

**BACKGROUND:** Some opioid medications are made from the opium poppy plant while others are made by scientists in labs. Opioids have been used for years to treat people who have had major surgeries including dental work, serious sports injuries, or cancer. When taken as prescribed, opioids are relatively safe and can reduce pain in the short term. But if a person misuses the drug and doesn't take them as prescribed, they can have dangerous consequences. The most commonly used prescription opioids are oxycodone (OxyContin®), hydrocodone (Vicodin®), codeine, and morphine. Heroin is an opioid, but it is not a medication. Fentanyl is a powerful prescription pain reliever, and is sometimes added to heroin by drug dealers, causing doses so strong that people can die from an overdose. An average of 1 in 100 young adults between the ages of 12 and 17 currently misuse prescription opioids, and 57% who misused them got them from a friend or relative. (Source: <https://www.drugabuse.gov/publications/opioid-facts-teens/faqs-about-opioids> and

**OPIOID ADDICTION AND SYMPTOMS:** Opioids make your brain and body believe the drug is necessary for survival. As you begin to tolerate the dose you've been prescribed, you may find that you need even more medication to relieve the pain, which can lead to dependency. Addiction takes hold of the brain and is far more complex and less forgiving than many people realize. It is recommended to talk to a physician anesthesiologist or other pain medicine specialist about using them safely and exploring alternative options if needed. People addicted to drugs may change their behavior. Some possible signs include mixing with different groups of people or changing friends; spending time alone and avoiding time with family and friends; losing interest in activities; being very tired and sad; eating more or less than usual; being overly energetic, talking fast and saying things that don't make sense; quickly changing moods; sleeping at odd hours; attending work or school on an erratic schedule; and experiencing financial hardship. (Source: <https://www.asahq.org/whensecondscount/pain-management/opioid-treatment/opioid-abuse/>)

**A PROMISING ALTERNATIVE:** An experimental compound with a dual action at two opioid receptors may provide powerful pain relief without many of opioids' harmful side effects. The new compound, called AT-121, may also have potential as a treatment alternative for opioid addiction. Dr. Nurulain Zaveri and colleagues at Astraera Therapeutics used medicinal chemistry, computer modeling, and structure-based drug design to develop AT-121. Like opioids such as morphine and oxycodone, AT-121 binds to the mu opioid receptor (MOR). However, unlike those opioids, AT-121 also binds to another opioid receptor called the nociceptin/orphanin FQ peptide (NOP) receptor. According to Dr. Zaveri, this interaction with the NOP receptor enhances AT-121's analgesic effect and blocks unwanted side effects often seen with current opioid medications. Dr. Huiping Ding, Dr. Mei-Chuan Ko, and colleagues at Wake Forest School of Medicine conducted preclinical tests of AT-121, and after confirming in vitro that AT-121 bound strongly to and activated both MOR and NOP receptors, the research team assessed its pain-suppressing efficacy. In one experiment, the researchers found that AT-121 at a dose of 0.03 mg/kg completely suppressed monkeys' discomfort when their tails were placed in warm water. To achieve the same level of pain suppression with morphine, a dose 100 times higher was required. In another experiment, AT-121 reduced heightened pain sensations like those that are sparked by hypersensitive pain fibers in some chronic pain conditions. (Source: <https://www.drugabuse.gov/news-events/nida-notes/2019/02/promising-alternative-to-opioid-pain-medications>)

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