WHITE PAPER

The Emerging Threat of Nitazenes in the Synthetic Opioid Crisis

Introduction

Nitazenes are a novel class of synthetic opioids that have recently emerged as a significant threat in the global drug market. Initially developed in the 1950s as analgesic agents, nitazenes were never approved for medical use. However, in recent years, they have entered illicit drug markets across North America, Europe, and other regions, raising alarms due to their extreme potency and increasing presence in overdose cases. With strengths ranging up to 40 times that of fentanyl, these substances pose a severe risk of fatal overdoses and are becoming a growing concern for law enforcement, medical professionals, and policymakers alike.

Background and Chemical Properties

Nitazenes belong to the 2-benzylbenzimidazole class of opioids and act as μ-opioid receptor agonists. Some of the most commonly encountered nitazenes include isotonitazene, metonitazene, and etonitazene, each exhibiting varying degrees of strength. Notably, etonitazene has been found to have potency comparable to carfentanil, a substance already notorious for its lethal potential. Nitazenes have been detected in various forms, including powders, counterfeit pills, vaping liquids, and nasal sprays, sometimes marketed as "fentanyl-free" opioids. However, their presence in counterfeit prescription drugs and adulterated heroin further exacerbates the risk of unintentional consumption and overdose.

Global Prevalence and Market Trends

Since their emergence in illicit drug markets, Nitazenes have been reported across multiple continents, including North America, Europe, South America, Asia, Africa and Oceania. In 2019, Nitazenes were increasingly detected in the illegal drug market, and by 2023, Nitazenes comprised 14% of all novel psychoactive substances reported to the United Nations Office on Drugs and Crime (UNODC), indicating a rapid rise in their circulation. In Dublin and Cork, Ireland, N-pyrrolidino etonitazene and N-pyrrolidino protonitazene were found in heroin, contributing to 77 overdose cases in late 2023. In Latvia and Estonia, Nitazenes were implicated in 25% and 50% respectively, of all drug-related deaths in 2023.

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Health Risks and Overdose Potential

The effects of nitazenes are similar to other opioids, including pain relief, euphoria, respiratory depression, nausea, and fever. However, due to their high potency, even small doses can cause fatal overdoses. Users have reported experiencing intense withdrawal symptoms and a strong compulsion to redose, which further increases the risk of addiction. Signs of a nitazene overdose include unconsciousness, slow or shallow breathing, blue lips or fingernails, and pinpoint pupils. While naloxone (Narcan) remains an effective reversal agent, multiple doses may be required due to the potentially prolonged effects of nitazenes.

Detection and Law Enforcement Challenges

Detecting nitazenes in illicit drug supplies remains a challenge due to the number of nitazenes and the fact that they are often mixed with other substances. Traditional fentanyl test strips do not detect nitazenes, requiring specialized test strips or other analytical instruments such as high-pressure mass spectrometry. Bulk detection devices that rely on Raman or FTIR technology, are often ineffective in detecting nitazenes because they are present at such low concentrations.

The MX908 has demonstrated effectiveness in identifying nitazenes at trace levels, providing a valuable tool for first responders and law enforcement agencies. Despite these advancements in the field, many jurisdictions do not routinely test for nitazenes in toxicology panels, leading to underreporting of their prevalence in overdose cases.

Case Study

During an arrest in the northeast United States, police officers discovered a plastic bag of “M30” pills suspected to be counterfeit oxycodone. Knowing these counterfeit pills commonly contain fentanyl, the officers analyzed the pills with several available technologies and received the following results:

Fentanyl test strips: Negative result. Despite these pills commonly containing fentanyl, the test strips were negative.

Raman analysis: Acetaminophen (Tylenol). The officers tried analyzing the pills using a handheld Raman and received a result of “Acetaminophen.” While not a controlled substance, this is suspicious as acetaminophen is not an active ingredient in oxycodone pills.

MX908: N-Pyrrolidino Etonitazene and Acetaminophen. Since nitazenes are so often present in extremely low concentrations, officers need a technology capable of identifying these drugs at trace levels. The MX908 was able to identify the nitazene present in the pills as well as the acetaminophen cutting agent.

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Regulatory and Policy Responses

In response to the rising threat, the U.S. Drug Enforcement Administration (DEA) has classified several nitazenes, including butonitazene, etodesnitazene, metonitazene, and N-pyrrolidino etonitazene as Schedule I controlled substances. Additionally, the United Nations has placed multiple nitazene analogs under international drug control measures. However, enforcement remains challenging due to the ability of illicit manufacturers to produce and ship these drugs while circumventing existing regulations. The affordability and availability of nitazenes on black market websites further complicate efforts to control their distribution.

Conclusion

The emergence of nitazenes represents a new and dangerous chapter in the synthetic opioid crisis. Their extreme potency, widespread availability, and increasing presence in overdose cases underscore the need for comprehensive strategies, including enhanced detection methods. Greater awareness among law enforcement, medical professionals, and the public is essential to mitigating the risks associated with these potent substances. Without urgent intervention, nitazenes have the potential to surpass fentanyl as the leading cause of opioid-related deaths worldwide.

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