**Xylazine adulterated fentanyl**

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Xylazine, an alpha-2 receptor agonist used in veterinary medicine for its sedative and muscle relaxant effects, has been reported in forensic toxicology casework since the 1980s. It is not approved for human use but is used as an adulterant in heroin and illicit fentanyl. Data from a large reference laboratory was used to monitor the prevalence and geographic spread of xylazine over a 3.5-year period. During this time period approximately 2.7% of 260000 blood specimens which underwent comprehensive toxicology screened positive for Xylazine. Positivity increased from less than 1% of screened cases in January 2019 to >4% in June 2022. Xylazine detections also spread geographically during this time period from 9 states in January 2019 to 45 states in Jun 2022. Xylazine was quantified in 6224 cases, over 99% of which also contained fentanyl. The mean ± SEM concentration in medicolegal death investigation cases was 38 ± 1 ng/mL which was not significantly different than the concentration in driving under the influence of drug cases (39 ± 4 ng/mL). After opioids, stimulants, phyto-cannabinoids and benzodiazepines were the most common drug classes detected in conjunction with xylazine in both DUID and MDI casework. In summary, xylazine exposure continues to increase, most through the adulteration of illicit opioids. There is extensive overlap in the concentrations between living and deceased individuals making it difficult to interpret the role of the drug in MDI or DUID cases without other case information.

**Navigating nitazenes: in vitro characterization and prioritization of 2-benzylbenzimidazole opioids**

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2-Benzy1benzimidazole ‘nitazene’ opioids are emerging on the recreational opioid market at a rapid pace. In this talk, we discuss how the use of an in vitro assay monitoring µ-opioid receptor (MOR) activation helps to determine structure-activity relationships that may shine a light on the potential danger of novel nitazene analogues.