

## Adulterants in drugs of abuse: a recent focus of a changing phenomenon

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### Abstract

The adulteration of drugs of abuse is a well-known practice with alarming public health implications. In fact, the presence of other substances than those declared by the drug dealers may expose the consumers to unexpected adverse effects, even potentially fatal ones depending on the adulterant. Various adulterants are often added during the manufacturing process as cutting agent for deliberate underdosing, such as in case of levamisole for cocaine, or to strengthen the drug effect, as in case of fentanyl for heroin. The authors aimed to elaborate on such unfolding dynamics and concluded that continuous development of effective analytical tools, along with a closely focused evaluation of each case by the medical doctor is essential to clarify the origin of the intoxications, so as to undertake the best therapeutic pathway. *Clin Ter* 2022; 173 (1):54-55. doi: 10.7417/CT.2022.2392

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Dear editor,

the adulteration of drugs of abuse is an old practice with alarming public health implications. In fact, the presence of other substances than those declared by the drug dealers may expose the consumers to unexpected adverse effects, even potentially fatal ones depending on the adulterant. The adulterants are often added during the manufacturing process as cutting agent for intentional underdosing, such as in case of levamisole for cocaine, or to enhance the drug effect, such as in case of fentanyl for heroin. However, the adulterants may induce not only a synergistic effect, resulting in a higher toxicity of both the substances, but they may act as primary toxic agent as well, exerting a multiple organ toxicity (1). On the other hand, minor toxic effects were reported in intoxications due to exposure to drug of abuse adulteration, such as vasculitis in chronic user or cocaine adulterated with levamisole (2,3).

Although this well-known issue was already described in the literature, recently acquired evidence suggests that the phenomenon still poses a major threat, with some changes introduced in the black market. Recently, a case of vasculitis related to levamisole exposure was reported. A 48 years-old man presented with acute bilateral pain and ear rush. The urinalyses provided positivity for cocaine, suggesting the eventual exposure to levamisole as adulterants. The toxicological analysis screening suggested to proceed with a punch biopsy to investigate the nature of the vasculitis that was confirmed as levamisole induced vasculitis (4).

Another relevant related issue is adulterated heroin, usually sold in mixture with other opioids, such as methorphan, or other xenobiotics such as paracetamol or caffeine (1).

More recently, different adulterants in heroin and opioids were found as primary cause of toxicity in several cases reported in the literature, especially due to the COVID-19 pandemic restrictions (5). In particular, the rapid increase of street heroin price made the substance inaccessible for the majority of usual abusers, who were compelled to divert to other substances. This was the case of a 28-years old man with a history of heroin abuse, who presented to telemedicine services in India with confusion and inability to walk, in July 2020 (6). Due to heroin shortages on the illicit market, the man began to add to the heroin a yellowish powder sold as “cut” to enhance the heroin effect and hence reduce the quantity of heroin in each dose. Although the symptoms upon admission were not ascribable to heroin acute intoxication, the medical doctors conducted toxicological screening that revealed the exposure to morphine and benzodiazepines. Finally, the “cut” was analysed through a GC-MS screening method confirming the presence of benzodiazepine (oxazepam, nordazepam, alprazolam, ketazolam), along with acetaminophen, caffeine, and unexpectedly methaqualone (6). To this concern, the methaqualone was reported as heroin cutting agent in the 80s, suggesting that the current COVID-19 crisis is pushing the manufacturer to resort to old excipients. Another old fashioned opioid cutting agent recently reemerged on to the illicit market. In fact, the vet-

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erinary sedative xylazine was used as heroin and speedball adulterant in the first decade of 2000 and it was reported as a new rising trend in North American illicit markets. Xylazine was recently detected in the toxicological analyses of a number of fentanyl related intoxications reported in Toronto, during a pilot drug checking program (7).

In addition to the self-administration of classic drug of abuse, adulteration may pose an unexpected danger also the unintentional drug consumer, such as in case of drug facilitated sexual assault or chem-sex. Significantly, a case of unintentional intake of sildenafil with g-hydroxybutyric acid (GHB) was reported in the literature (8).

Evidently, the toxicological analyses played a crucial role in the above reported cases, in which the alleged adulterant disguised the effects of the consumed drug of abuse and resulted in more toxic effects (9). The evidence of changes in drug adulteration trends should raise the attention of the scientific community, since new challenges appears to emerge for the toxicologist and toxicology laboratory analysts. Moreover, the unconventional matrices screening was proven to be an effective tool to detect exposure to psychoactive substances (10). In this concern, the evaluation of alternative matrices may represent an upgrade activity to reveal unexpected substances, such as the adulterants. Finally, the continuous development of effective analytical tools, along with a closely focused evaluation of each case by the medical doctor is essential to clarify the origin of the intoxications, so as to undertake the best therapeutic pathway.

**Conflict of interest:** The authors declare that there is no conflict of interest regarding this manuscript.

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