H127 Levamisole: A High-Performance Cutting Agent

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After attending this presentation, attendees will better understand the mechanisms of action of cocaine and amphetamines and will learn about the physical, chemical, and pharmacologic properties that have made the anthelminthic agent levamisole one of the most unlikely and widely encountered cocaine adulterants. Attendees will also be acquainted with the possible role of levamisole in cocaine-related fatalities.

This presentation will impact the forensic science community by reviewing the rise of levamisole as a cocaine adulterant and explain the properties of the chemical that almost make it the perfect cocaine cutting agent. An argument will be made for screening of the compound in cocaine-related fatalities to more accurately determine cause of death in these cases. Cocaine cut with levamisole has been associated with a number of deaths; the role levamisole plays in these deaths should be considered.

Drugs like cocaine and amphetamines are abused because of their stimulatory effects. Illicit drugs are frequently diluted (cut) with a variety of materials prior to sale/resale to bulk up the product and increase profit.[1,2] Adulterants are generally selected due to their physical resemblance to cocaine, low cost, or added physiological effects.[2,3] One such adulterant is the imidazothiazole derivative levamisole, an amphetamine and anthelminthic agent acting as a ganglion stimulant in mammals and a depolarizing muscular blocker in nematodes (roundworms).[4,5] Although marketed for numerous uses in humans, including an appetite suppressant, immunomodulatory agent, and antineoplastic agent, it was withdrawn from the United States market in 2000 due to side effects; it is currently marketed only for veterinary purposes as an anthelminthic.[1,4,6-8] Recent estimates suggest that the proportion of cocaine laced with levamisole may now be higher than 80%.[9,10]

In vivo, levamisole is metabolized to aminorex, which is bioactive.[1] The potency of aminorex has been found to be comparable to cocaine, and aminorex's amphetamine-like properties may be responsible for levamisole's psychostimulant effects.[1] Levamisole also readily crosses the Blood Brain Barrier (BBB) and has a longer half-life than cocaine.[1] Through various biochemical mechanisms, levamisole prolongs the action and potentiates the effects of cocaine and may continue to provide amphetamine-like stimulation after the direct effects of cocaine have worn off.[1,4,7,11] Additionally, levamisole is inexpensive relative to other potential adulterants, increasing cocaine profits.[4,9,12] These features make levamisole (and aminorex) an attractive choice as a cocaine additive.[1]

Levamisole use can present with a number of adverse effects, include nausea and vomiting, headache, fatigue, fever, diarrhea, myalgia, dizziness, confusion, and rash.[13] Serious complications include agranulocytosis, leukopenia, thrombocytopenia, vasculopathy and vasculitis, dermal necrosis, leukoencephalopathy, psychosis, pulmonary hypertension and hemorrhage, glomerulonephritis, emboli, arthritis, Coronary Artery Disease (CAD), and circulatory collapse.[1,4,13,14] Some of these complications appear to be associated with levamisole's propensity to provoke hypersensitivity reactions in people with certain genetic predispositions.[7,11] Such reactions have been reported previously, with reoccurrence of symptoms after re-exposure.[11] Reviews on immunologic associations note the presence of Anti-Neutrophil Cytoplasmic Antibodies (ANCA), including perinuclear ANCA (pANCA), cytoplasmic ANCA (cANCA), and type III cryoglobulinemia.[11,14] Given its association with so many potentially deadly side effects, it is not surprising that numerous fatalities, typically attributed to pathology of the heart, brain, or lungs, have been linked to levamisole exposure through tainted cocaine.[7,8,15-18]

Easy to obtain, inexpensive, physically similar in presentation, and with the inherent ability to potentiate and perpetuate the effects of the primary agent, levamisole seems the perfect choice for maximizing profit while leaving consumers none the wiser, except in those cases with deadly consequences. Cause of death in patients with cocaine and levamisole intoxication may be due to any number of mechanisms, ultimately severely impacting the heart, lungs, and brain. Given its prominence as a cocaine additive, its presence in a majority of cocaine specimens evaluated in numerous centers around the world, its known side-effect profile and its role in autoimmune reactions, and its potential role in facilitating or exacerbating pathological processes leading to sudden death, toxicological screening for levamisole is an important element in the analysis of suspected cocaine-related fatalities.

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