



K43 Postmortem Distribution of Nicotine and Cotinine in Suicidal Overdoses Following Transdermal and Oral Administration

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Learning Overview: After attending this presentation, attendees will have a better understanding of the postmortem distribution of nicotine and cotinine following transdermal and oral administration.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by providing medical examiners and toxicologists with postmortem concentrations for nicotine and cotinine in suicidal overdoses following transdermal and oral administration.

Nicotine is a toxic alkaloid present in tobacco at concentrations (w/w) of 0.5%–8%. In addition to cigarettes and smokeless tobacco products, nicotine is commercially available in lozenges, sublingual tablets, chewing gum, nasal sprays, inhalers, transdermal patches, and solutions for electronic smoking devices. Nicotine produces stimulation of nicotinic receptors in the autonomic ganglia and central nervous system. Nicotine overdose produces symptoms ranging from nausea, dizziness, tachycardia, and hypertension to convulsions, coma, and death. Blood nicotine concentrations ranging from 1.0mg/L to >100mg/L have been reported in nicotine associated fatalities.¹

The Office of the Chief Medical Examiner (OCME) of the State of Maryland recently investigated two deaths due to nicotine intoxication; one involving transdermal administration and the other involving oral ingestion of a vape liquid.

Case 1 History: A 60-year-old female was found unresponsive in her residence during a welfare check (requested by friends who had received suicide letters mailed by the decedent). She was lying in a supine position on her bed with a suicide note located on the bedside table. Two empty, unlabeled pill bottles and a taped recording of the decedent were also located in the bedroom. Due to case history, an inspection at OCME was performed. External examination revealed 14 21mg/24hr nicotine patches on her body (ten on her chest, one on each arm and leg). Other than the nicotine patches, inspection findings were unremarkable. Comprehensive toxicology testing was performed, and the results are summarized in the table below.

Case 2 History: A 34-year-old female was found unresponsive in the driver’s seat of a vehicle parked in a residential neighborhood. She had been reported missing two days earlier by her mother who reported that the decedent indicated that she was going to kill herself by “poisoning.” Five empty bottles of Big Heart 555 vape liquid (12mg/34mL) and an empty water bottle were present in the vehicle. A full autopsy was performed, and findings were unremarkable. Comprehensive toxicology testing was performed, and the results are summarized in the table below.

Comprehensive toxicology testing included volatiles, an acidic neutral drug screen, an alkaline drug screen and Enzyme-Linked Immuno-Sorbent Assay (ELISA) for morphine, benzodiazepines, and oxycodone. Nicotine was confirmed and quantitated by liquid-liquid extraction, followed by Gas Chromatography/Mass Spectrometry (GC/MS). Briefly, internal standard (d₄-Nicotine; 0.2 mg/L) was added to specimens (5.0mL) that were alkalized with 0.1N sodium hydroxide and extracted with n-butyl chloride, then back extracted into 0.1N sulfuric acid, and finally alkalized with ammonium hydroxide and extracted into methylene chloride. Isopropanol (100µL) was added and the extract was evaporated to the isopropanol layer which was injected into the GC/MS for analysis. The method was linear from 0.12mg/L to 2.0mg/L for nicotine and cotinine. A five-point calibration curve and two control concentrations (0.30mg/L and 1.25mg/L) were used for quantitation. An administrative reporting limit of 0.12mg/L for both analytes was used. Toxicology results (mg/L or mg/kg) for the two cases are summarized below.

Case	Heart Blood	Peripheral Blood	Liver	Kidney	Vitreous Humor
1	Nicotine: 0.20	Nicotine: 0.22	N/A	N/A	Nicotine: 0.12
	Cotinine: 0.36	Cotinine: 0.48			Cotinine: 0.32
	Alprazolam: 0.033				
	Dextromethorphan: 0.5				
	Diphenhydramine: 0.6				
	Fluoxetine: 1.1				
	Hydroxyzine: 0.4				
2	Oxycodone: 1.2				
	Nicotine: 34	Nicotine: 21	Nicotine: 170	Nicotine: 31	Nicotine: 9.9
	Cotinine: 0.40	Cotinine: 0.30	Cotinine: 1.2	Cotinine: 0.35	Cotinine: <0.6
	Diphenhydramine: 0.05				

For Case 1, the medical examiner ruled that the cause of death was nicotine, oxycodone, fluoxetine, and dextromethorphan intoxication; the manner of death was suicide. For Case 2, the medical examiner ruled that the cause of death was nicotine intoxication; the manner of death was suicide. The nicotine concentrations detected in these two cases are significantly elevated from what would be expected with appropriate use of the products involved. In Case 1, it is likely that higher nicotine concentrations were not observed due to the presence of additional drugs at toxic concentrations and the slower transdermal route of administration. In Case 2, the nicotine concentration was very high with lower concentrations of cotinine, suggesting that death occurred quickly after administration of an excessive dose.

Reference(s):

¹. Baselt R.C. *Disposition of Toxic Drugs and Chemicals in Man*, 11th ed, (2017) 1521-1525.

Nicotine, Postmortem, Overdose