**Acetylfentanyl**

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\text{Acetylfentanyl} \quad (\text{phenylethyl-4-piperidyl-N-phenylacetamide})
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**Occurrence and Usage.** Acetylfentanyl (phenylethyl-4-piperidyl-N-phenylacetamide) is a synthetic fentanyl analogue that has been encountered as an illicit narcotic analgesic since 2013. It is usually supplied as the hydrochloride salt in powders or tablets for oral administration, nasal insufflation or intravenous injection. Doses of 300–3000 µg are said to produce effects lasting 2–6 hours.

**Blood Concentrations.** Blood or plasma levels of acetylfentanyl in recreational users of the drug have not been reported.

**Metabolism and Excretion.** Acetylfentanyl was shown using human hepatocyte preparations and authentic human urine specimens to undergo biotransformation via N-dealkylation, mono- and di-hydroxylation, dihydrodiol formation, amide hydrolysis and methyl, glucuronide or sulfate conjugation to a series of at least 32 metabolites (Watanabe et al., 2017). Incubation in a human liver microsomal preparation resulted in the formation of acetylnorfentanyl. Rats given a single intravenous 3 mg/kg injection developed peak urinary concentrations at 3 hours of 17 mg/L for both the parent drug and acetylnorfentanyl (Patton et al., 2014).

Acetylfentanyl exhibits postmortem redistribution; heart/peripheral blood concentration ratios in 6 deaths averaged 1.4 (range, 0.8–2.3) (Poklis et al., 2015; Fort et al., 2016).

**Analysis.** Acetylfentanyl exhibits a high degree of cross-reactivity in certain commercial immunoassays targeted at fentanyl (Wang et al., 2014; Tiscione and Wegner, 2017). Acetylfentanyl and acetylnorfentanyl have been quantitated in biological specimens by LC-MS (Patton et al., 2014; Poklis et al., 2015).

Acetylfentanyl was stable in serum for 2 weeks at room temperature and 1 month at 4 or -20 °C; it was stable in blood for 1 month at all 3 temperatures (Buzby et al., 2016).

**Toxicity.** Excessive doses of acetylfentanyl may cause drowsiness, respiratory depression, hypotension, seizures and coma. Six adults treated for acetylfentanyl overdose had serum and urine acetylfentanyl concentrations within 3–12 hours of admission of 4.7–52 and 31–235 µg/L, respectively (Helander et al., 2016).

At least 40 deaths involving acetylfentanyl were reported in the U.S. during 2013 (MMWR, 2013; Stogner, 2014). Twenty-two adults who died due to acute overdose with the drug had postmortem peripheral blood and urine acetylfentanyl levels of 89–945 and 41–9825 µg/L, respectively (Winecker, 2014; Finkelsen et al., 2015; McIntyre et al., 2015; Zhang et al., 2015; Cunningham et al., 2016). In 69 additional fatalities, postmortem blood acetylfentanyl concentrations ranged from 0.6–2100 µg/L (Isenschmid et al., 2014; Poklis et al., 2015; Fort et al., 2016; Kronstrand et al., 2016; Stockham et al., 2016; Takase et al., 2016; Dwyer et al., 2018).

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**References**


