Diethylpropion Concentrations in a Fatal Case (mg/L or mg/kg)

<table>
<thead>
<tr>
<th></th>
<th>Blood</th>
<th>Liver</th>
<th>Bile</th>
<th>Kidney</th>
<th>Injection Site</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5.4</td>
<td>0.9</td>
<td>14</td>
<td>0.9</td>
<td>43</td>
</tr>
</tbody>
</table>

**Analysis.** Determination of diethylpropion and its metabolites in biofluids has been accomplished by gas chromatography with detection by flame-ionization (Testa and Beckett, 1972; Dangor et al., 1986) or mass spectrometry (Wright et al., 1975; Rossi et al., 2010). Liquid chromatography-mass spectrometry has also been utilized (Sorensen, 2011).

Diethylpropion lost approximately 40% of its initial value in fluoridated blood stored for 5 days at room temperature, but it was stable for 6 days at 5 °C (Sorensen, 2011). Diethylpropion was stable in plasma for 3 weeks at 4 °C; it was stable in urine adjusted to pH 5 for 3 weeks at 4 °C, but exhibited instability at higher pH values (Dangor et al., 1986). It was stable in urine for 3 months at -20 °C (Rossi et al., 2010).

**References**


**Diethyltoluamide**

$t_{1/2}$: 2.5 h

$V_d$: 2.1 L/kg

$F_b$: 0.05–0.10

$b/p$: ?

CAS: 134-62-3

MW: 191.27 (C\textsubscript{12}H\textsubscript{17}NO)

**Occurrence and Usage.** Diethyltoluamide (N,N-diethyl-m-toluamide, DEET, Repel) is a synthetic organic liquid (b.p., 160 °C) used since 1957 as an insect repellent. It is available for consumer use in the form of lotions, sprays and sticks containing 5–95% of the active ingredient as the neutral substance and is intended for application to skin or clothing.

**Blood Concentrations.** Background serum DEET concentrations averaged 3.2 µg/L (range, 1.8–19) in 138 pregnant U.S. women during 2003–2004 (Barr et al., 2010). The application of 12–15 mg of DEET to the skin of 12 healthy men resulted in absorption of an average of 5.6% of the dose within 8 hours when undiluted technical-grade chemical was used, and 8.4% of the dose when 15% DEET in ethanol was applied (Selim et al., 1995). Serum DEET concentrations reached peak values of 0.3–1.0 mg/L within 1–4 hours after dermal application of 0.14–1.86 g of the chemical to 7 adult male volunteers (Smallwood et al., 1992). In a study involving a single adult male subject, a blood DEET concentration of 3.0 mg/L was reported 8 hours after dermal application of 10 g (Wu et al., 1979).

**Metabolism and Excretion.** DEET undergoes extensive biotransformation in man, with the production of at least 6 urinary metabolites. The known pathways include aromatic ring hydroxylation and conjugation, oxidation of the methyl group to a hydroxyl or carboxylic acid function, and mono- or di-N-deethylation. Urinary excretion of a
Diethyltoluamide labeled dose reaches a peak at about 16 hours after dermal application of DEET, and continues for many days. Urinary elimination accounts for an average of 5.6% of a labeled dose within 48 hours (Blomquist and Thorsell, 1977; Wu et al., 1979; Selim et al., 1995). In one experiment with adult male volunteers, only 2 of 5 individuals had detectable (0.09 mg/L) urinary levels of unchanged DEET in the first 24 hours after dermal application of 0.14–1.86 g, ranging from 0.3–2.0 mg/L (Smallwood et al., 1992).

Toxicity. Excessive dermal administration of DEET may result in toxic encephalopathy characterized by headache, agitation, irritability, confusion, disorientation, ataxia and convulsions. Reports of this syndrome primarily involve infants and young children, and sometimes describe a fatal outcome (Zadikoff, 1979; de Garbino et al., 1983; Lipscomb et al., 1992; Briassoulis et al., 2001). In one such case, a highly agitated young man had a serum DEET level of 1.6 mg/L at 16 hours post-admission (Hampers et al., 1999). Persons who survived the accidental or intentional oral ingestion of as much as 48 g of the chemical have experienced coma, hypotension, respiratory depression and tachycardia (Tenenbein, 1987). One such person, a 19 year old female who ingested as much as 24 g, had peak serum and urine DEET concentrations of 63 and 3.1 mg/L, respectively, at 2 and 24 hours post-ingestion; the serum DEET levels declined with an apparent elimination half-life of 2 hours (Fraser et al., 1995).

The following postmortem concentrations were found in 2 adults who died after intentionally ingesting 48 g of DEET (Tenenbein, 1987; Singer and Jones, 1993):

<table>
<thead>
<tr>
<th>DEET Concentrations in Fatal Cases (mg/L or mg/kg)</th>
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<tbody>
<tr>
<td>Blood</td>
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<tr>
<td>-------</td>
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<tr>
<td>Case 1</td>
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<tr>
<td>Case 2</td>
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</tbody>
</table>

Analysis. DEET has been analyzed in biological specimens by gas chromatography with nitrogen-selective (Crowley et al., 1986) or mass spectrometric detection (Fraser et al., 1995; Cherstniakova et al., 2006). Liquid chromatography with ultraviolet (Smallwood et al., 1992) or mass spectrometric detection (Olsson et al., 2004) has also been employed. DEET was stable in serum for 2 weeks at 4 °C and in urine for 1 week at 4 °C (Smallwood et al., 1992). It was stable in plasma for 1 year at -80 °C (Cherstniakova et al., 2006).

References


