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Case Report

# Poisoning suicide with ingestion of the pyrethroids alpha-cypermethrin and deltamethrin and the antidepressant mirtazapine: A case report

Vassiliki A. Boumba*, Georgios N. Rallis, Theodore Vougiouklakis

*Laboratory of Forensic Medicine & Toxicology, Faculty of Medicine, School of Health Sciences, University of Ioannina, 45110 Ioannina, Greece*

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ABSTRACT

This case report describes a death attributed to the intake of the pyrethroid insecticides, alpha-cypermethrin and deltamethrin, and the antidepressant mirtazapine. The autopsy findings showed absence of external traumatic injuries and internal generalized visceral congestion, edema and cyanosis. The toxicological results revealed the presence of a toxic concentration of mirtazapine (12.5 mg/L and 10.7 mg/L in blood and urine, respectively) and high concentrations of pyrethroids (2.46 mg/L alpha-cypermethrin and 2.40 mg/L deltamethrin in blood, and 0.41 mg/L alpha-cypermethrin and 0.46 mg/L deltamethrin in urine, respectively). Blood ethanol concentration was 0.75 g/L. All the evidence – from autopsy, police investigation and toxicology – was consistent with the intentional self-harm of the deceased. The current case was determined and recorded as a poisoning suicide. Cause of death of the deceased was reported as the synergistic toxicity of the ingested pyrethroids and mirtazapine. The presence of a significant blood ethanol concentration was considered a secondary contributory factor to the fatal outcome. The case presented herein is the first death attributed to poisoning from ingestion of pyrethroids in combination with mirtazapine, with the intention of the victim to cause self-harm, with corresponding toxicology results.



## 1. Introduction

Pyrethroids are a class of insecticides typically classified as synthetic pyrethrins. There are two classes of pyrethroids, type I and type II, that differ in chemical structure and in symptomatology [1]. Type II pyrethroids include the insecticides cypermethrin, and deltamethrin. Alpha-cypermethrin consists of two of the eight stereoisomers comprising cypermethrin, see Fig. 1a–1b [2]. Similarly, deltamethrin is a single stereoisomer of the eight theoretical stereoisomers corresponding to the molecular structure shown in Fig. 2 [3]. Alpha-cypermethrin is a highly active, broad spectrum insecticide, which is sprayed on plants to deter and eliminate pests, while deltamethrin is classified as a moderately hazardous insecticide.

The mechanisms by which pyrethroids cause toxicity are complex. The main effects of pyrethroids are achieved through action on sodium and chloride channels [4,5]. They act on nerve membranes by delaying the closing of the activation gate for the sodium ion channel (neurotoxic agents). Type II pyrethroids induce "long-lasting" inhibition of the sodium channel activation gate; meaning that a sodium channel exposed to a type II pyrethroid can remain open much longer; up to several seconds [6]. This results in prolonged permeability of the nerve to sodium and produces a series of repetitive nerve signals in sensory organs, nerves, and muscles. Type II pyrethroids also decrease chloride currents through voltage-dependent chloride channels. At relatively high concentrations, pyrethroids can also act on GABA-gated chloride channels, which may be responsible for the seizures seen with severe type II poisoning. Pyrethroids are some 2250 times more toxic to insects than mammals due to the increased sodium channel sensitivity, smaller body size and lower body temperature seen in insects. In addition, mammals are protected from toxicity by poor dermal absorption and rapid metabolism to non-toxic metabolites [2,3,7].

Despite their extensive use world-wide, there are relatively few reports of human unintentional acute poisonings due to exposure to pyrethroids [6,8–11] either at workplace [6,11] or at home

* Corresponding author.
*E-mail addresses:* vboumba@uoi.gr, vassiliki.boumba@monash.edu, vassiliki.boumba@gmail.com (V.A. Boumba).

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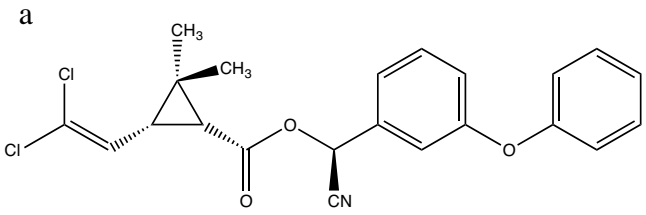
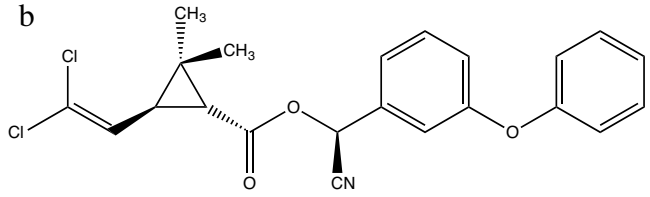



Alpha-cypermethrin




Alpha-cypermethrin

**Fig. 1.** Alpha-cypermethrin is a mixture of two stereoisomers which have the IUPAC names: (*S*)-cyano-3-phenoxyphenyl-(1*R*,3*R*)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane-carboxylate, shown in Fig. 1A and (*R*)-cyano-3-phenoxyphenyl-(1*S*,3*S*)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane-carboxylate, shown in Fig. 1B.

environment [6,8–10]. Most patients recovered within six days, however one study reported seven fatalities among 573 cases [6] while another reported one death among 48 cases [8].

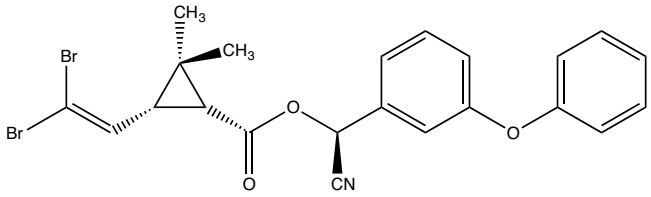
Mirtazapine is an antidepressant that acts as a strong α2 antagonist (enhancing noradrenergic and serotonergic neurotransmission without inhibiting serotonin re-uptake) and in overdosage may cause disorientation, drowsiness, and tachycardia [12]. Mirtazapine is considered as a relatively safe drug with respect to overdose with only a limited number of deaths reported due to mirtazapine overdose [13].

The case presented herein is the first published case of attributed to poisoning from ingestion of pyrethroids, with the intention of the victim to cause self-harm, in combination with mirtazapine, with corresponding toxicology results.

## 2. Methodology

### 2.1. Case background

A 52-year-old male was found dead in the bathroom of his home. At the scene found next to the body were two white plastic bottles with traces of white emulsion on the inner walls, two empty glasses with traces of white emulsion and small grounds of a white/bluish powder of which one glass contained a spoon. The two plastic bottles were labeled as insecticide formulations: the label of one box was “deltamethrin 1.5% w/v, total volume 160 mL”, and the label of the other one was “alpha-cypermethrin 6% w/v, total volume 50 mL”. An autopsy was performed about 24 h after discovery of the body at the Laboratory of Forensic Medicine & Toxicology, Faculty of Medicine, University of Ioannina. The external examination of the body revealed the absence of traumatic injuries and also early signs of putrefaction and cyanosis. The internal examination revealed generalized visceral congestion and edema. The stomach contained a greenish fluid of about 300 mL, five round yellowish tablets (about 0.8 cm in diameter) and remnants of tablets. Postmortem specimens retrieved at autopsy, cardiac blood (in blood tubes with sodium fluoride as preservative), urine and stomach contents (tablets and stomach




Deltamethrin

**Fig. 2.** The structure of the molecule of deltamethrin which has the IUPAC name [(*S*)-cyano-(3-phenoxyphenyl)-methyl] (1*R*,3*R*)-3-(2,2-dibromoethenyl)-2,2-dimethyl-cyclopropane-carboxylate.

fluid were put in separate containers), and also the paraphernalia collected at the scene by the police were sent for toxicological analyses.

### 2.2. Materials for toxicological analysis

Ethanol and volatiles analysis was performed in whole blood by head space gas chromatography flame ionization (HS-GC-FID) detection [14]. Toxicological screening for the presence of common drugs and poisons was carried out by a routine gas chromatography–mass spectrometry (GC–MS) technique in full-scan mode on extracts of blood and urine, after solid phase extraction (Chem Elut cartridges, Agilent Technologies, Lake Forest, CA, USA), and on extracts of the gastric contents, the tablets isolated from gastric contents and the traces isolated from the paraphernalia, after liquid–liquid extraction. GC–MS analyses were performed using a Shimadzu GC17A-QP5050 GC–MS instrument equipped with an Equity5 column (30 m × 25 mm id), 95% dimethyl-5% diphenylpolysiloxane, film thickness 0.25 μm, purchased from Supelco (Bellefonte, PA). Helium was employed as the carrier gas at a constant pressure of 23.24 psi. For the screening analyses the GC oven temperature was programmed to rise from 60° to 280 °C using a step-temperature program and the total run time was 36.17 min. The GC injector and transfer line were maintained at 260 °C and the injector was operated in the split less mode. Full scan spectra were acquired in the interval 40–550 amu operating in the EI mode at 70 eV. Screening for opiates, benzodiazepines, amphetamines, cannabinoids and cocaine metabolites in urine and blood was performed by immunoassays (SYVA, Abbott Park, IL). The confirmation and quantification of mirtazapine (purchased from Lipomed) was performed by GC–MS on the selected ion monitoring (SIM) mode using the ion (m/z) 195, 180 and 208 for the identification and the m/z = 195 for its quantification in blood and urine as described previously [15]. The method was adapted for urine as suggested by the FDA guidelines [16].

### 2.3. Alpha-cypermethrin and deltamethrin identification and quantification by GC–MS-SIM

Standard alpha-cypermethrin and deltamethrin solutions in concentrations 1 mg/mL in methanol were purchased from Chem Service (West Chester, PA). Working standards of pyrethroids were prepared in methanol.

The determination of alpha-cypermethrin and deltamethrin in blood and urine was performed following a procedure described previously [17,18] for the determination of pyrethroids in blood. The procedure was suitably adapted and validated for use in the current case. The applied procedure for sample (blood and urine) preparation was as follows: 1 mL blood or urine was mixed with 5 ml of *n*-hexane-acetone (8:2 v/v) and the mixture was rigorously vortexed for 10 min. After settling for 5 min the mixture was