Propoxyphene Overdosage:  
A Study of Cases Involving Analgesic Preparations Containing Dextropropoxyphene

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Abstract. Propoxyphene and paracetamol concentrations have been determined in blood, urine, liver blood and stomach contents from 17 post mortem cases in which Distalgesic (a propoxyphene and paracetamol compound preparation) was involved. Five patients admitted to hospital with suspected Distalgesic poisoning have also been investigated. In most cases the propoxyphene concentrations, but not the paracetamol concentrations, exceeded the minimum lethal levels reported. On the basis of our results it appears that of the constituents of Distalgesic, propoxyphene has a far more immediate and dangerous effect than paracetamol.

Key words: Propoxyphene — Paracetamol — Distalgesic — Gas liquid chromatography — Fatal poisoning.

Several reports have appeared in recent years on the toxic properties of propoxyphene (Worm, 1971; Sturner and Garriott, 1973; Baselt et al., 1975). These reports have almost invariably dealt with the risks involved from preparations containing either propoxyphene hydrochloride (Darvon, Abalgin) or propoxyphene napsylate (Darvon N) as the active constituent.

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In the United Kingdom, the most commonly prescribed preparation is one containing a mixture of paracetamol, 325 mg, and dextropropoxyphene hydrochloride, 32.5 mg (Distalgesic). This preparation has recently been used in an increasing number of suicide attempts and toxicological data is presented from a number of cases examined in the Department of Forensic Medicine at Charing Cross Hospital, London.

Following oral ingestion propoxyphene (4-dimethylamino-3-methyl-1,2-diphenyl-2-butanol propionate) is initially concentrated in the liver and lung and then undergoes hepatic N-demethylation to norpropoxyphene (McMahon et al., 1971). It is mostly excreted in the bile, either free or as a conjugated metabolite. Total urinary excretion is low. Human urine has been found to contain several minor metabolites. The toxicity of norpropoxyphene is comparable to that of propoxyphene in experimental animals (Nickander and Smits, 1973) and is partly responsible for the pharmacological effects of propoxyphene. Further N-demethylation and re-arrangement of norpropoxyphene produces dinorpropoxyphene but only trace amounts of the latter are present in plasma.

There is some variation in the literature with regard to toxic levels of propoxyphene in blood. Death has resulted from the ingestion of 0.5—0.8 g of propoxyphene yet survival has been noted after a presumed ingestion of 6.5 g of propoxyphene hydrochloride and 9.0 g of propoxyphene napsylate. The first fatal propoxyphene hydrochloride poisoning was reported by McCarthy and Kennan (1964). Since then there have been several cases in which propoxyphene poisoning has caused death or been a contributory factor.

Cravey et al. (1974) found fatal propoxyphene concentrations in blood to be in the range 2—58 µg/ml whereas McBay et al. (1974) reported 2—20 µg/ml to be present in blood. Baselt et al. (1975) detected blood concentrations of propoxyphene between 0.4 and 8.3 µg/ml in fatalities attributed to propoxyphene alone, 0.4—2.4 µg/ml in combined alcohol and propoxyphene deaths and 0.04—10.4 µg/ml in cases where other drugs were also involved. Worm (1971) studied nine cases of fatal poisoning and found higher blood concentrations. Kopjak and Finkle (1976) and Jejurikar et al. (1976) have also recently investigated propoxyphene overdoses.

To date investigations into propoxyphene overdoses appear to have been confined to those involving Darvon and Abalgin preparations. To our knowledge little has been published on deaths due to ingestion of Distalgesic preparations. The present study is concerned with 17 fatalities in which death was attributed wholly or in part to Distalgesic. Two cases in which the subjects survived after ingestion of toxic amounts of Distalgesic are also investigated. In three other instances ante mortem blood samples were analysed from patients who subsequently died from propoxyphene poisoning.

**Experimental**

The analytical techniques used included thin layer chromatography, gas liquid chromatography and spectrophotometry.

A variety of toxicological screening procedures for drugs and chemicals were performed: