

for analgesia"—pain relief—the levels of nor-propoxyphene causing inhibition in these dogs were the same 1 to 3 micrograms per milliliter range which can be seen in people who are chronically using the drug.

For the first time in the current labeling of Darvon there is mention, 2 years after the study was done, of the possibility of cardiac conduction problems.

There is no mention of nor-propoxyphene, the fact it accumulates, or that there is evidence of this.

It just says problems can occur with the drug.

A recently published Danish study¹ also shows that nor-propoxyphene in the 1 to 3 micrograms per milliliter range in rabbits can cause significant delay or inhibition of cardiac conduction and cardiac arrhythmias also were seen.

An earlier Danish study of 11 cases of Darvon poisoning² showed that four patients had cardiac conduction delays similar to those described above with blood nor-propoxyphene and propoxyphene levels of:

<i>NPX</i>	<i>PX</i>
0.78 -----	0.47
.39 -----	.74
.79 -----	.51
.35 -----	.23

In other words, they had more of the metabolite than of the drug itself in their blood.

One of the four patients also ingested a substantial amount of alcohol, but this in itself is not known to cause the cardiac delays.

According to both Dr. Larry Lewman, deputy coroner of Oregon, and Dr. Boyd Stevens, coroner of San Francisco, most of the Darvon deaths are not suicides but accidents.

One of the criteria for making this decision is a nor-propoxyphene blood level as high or higher than the propoxyphene level, often suggesting chronic use of propoxyphene.

Blood nor-propoxyphene levels in such accidental deaths are often slightly less than 1 microgram, 1, 2, 3, or 4 micrograms per milliliter of blood with propoxyphene levels often less than 1.

The margin of safety or the therapeutic index of a drug is the ratio between the amount needed to achieve the therapeutic effect (in this case alleged relief of pain) and the amount causing toxicity.

According to Danish toxicologist, Dr. J. Simonsen³ Darvon has a "narrow therapeutic index": He says that "just four times the ordinary therapeutic dose can produce highly serious poisoning."

The experience concerning Darvon varies from one part of the country to the other.

In North Carolina, they published studies suggesting most deaths are suicides, but even in a paper by Dr. McBay, who will testify later, one of his patients had a blood level of propoxyphene of 0.8, and a level of nor-propoxyphene of 2, suggesting in fact they had not in fact taken a huge suicidal dose, and several of their patients are also listed as accidents rather than suicide.

¹ Lund-Jacobsen, *Acta. pharmacol. et toxicol.*, 42, 171, 1978.

² Gustafson and Gustafson, *Acta. Med. Scand.* 200, 241, 1976.

³ *Ugeskr. Laeg.* 137(44) 2605-2609, 1975.