Propoxyphene hydrochloride was administered orally to four dogs every eight hours for nineteen days. The initial dose was 20 mg/kg, three times daily, an amount ten to twelve times the recommended human dose. This dose was increased to 60 mg/kg three times daily in increments of 5 to 15 mg/kg every three or four days. The dogs remained ambulatory, but anorexia, tremors, emesis, and sedation were noted periodically.

Plasma concentrations of propoxyphene, $2.3 \pm 0.5$ micrograms/ml, and norpropoxyphene, $18.4 \pm 4.7$ micrograms/ml, were greater than those generally regarded as lethal in man. Tissue concentrations were in excess of plasma concentrations.

Electrocardiograms showed a 10- to 30-percent increase in the PR interval (A-V conduction time) with the initial dose. However, there was no further increase in the PR interval until after the 60-mg/kg dose was reached. At this high dose a moderate tachycardia (132/minute) and increased amplitude of P, QRS, and T waves were noted.

## Summary

The possibility that the effects of norpropoxyphene on cardiac conduction play a role in propoxyphene toxicity