recognize is that norpropoxyphene concentrations reach a plateau at which they remain, given a constant dosage situation. This plateau, reached in four or five half-lives, or about 120 hours, results from an equilibrium state wherein rates of excretion and synthesis of norpropoxyphene (by hepatic demethylation of propoxyphene) are equal.

If chronic norpropoxyphene toxicity exists, it would most likely reflect its local anesthetic effects on myocardial conduction.

In a study conducted at the Lilly Clinic, Wishard Memorial Hospital, Indianapolis, electrocardiograms were constantly recorded on Holter monitors during chronic propoxyphene administration to two male volunteers, ages fifty-six and sixty. After a six-day control period a single 300 mg dose of propoxyphene napsylate was given, and blood samples were obtained at various intervals over the next forty-eight hours. Maximum concentrations of propoxyphene and norpropoxyphene observed in these two subjects were 0.25 and 0.37 (propoxyphene) and 1.1 and 1.4 (norpropoxyphene) micrograms/ml, respectively. From day 9 through day 15 the subjects received propoxyphene napsylate 100 mg every four hours (i.e., 600 mg/day). Day 16 through day 25 served as the posttreatment control period. Neither subject manifested

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