

the napsylate) were noted at about 120 hours, i.e., at about four norpropoxyphene "half-lives."

Single daily doses of 125 mg norpropoxyphene administered to humans for seven days resulted in peak plasma concentrations of norpropoxyphene of 0.25 to 0.55 micrograms/ml and elicited no overt adverse effect.

The toxicological effects of propoxyphene relate to its analgesic (CNS) properties, which are shared to a much lesser degree by norpropoxyphene, and are readily reversed by antagonists such as naloxone. The local anesthetic properties, shared by both propoxyphene and norpropoxyphene but to a greater extent by norpropoxyphene, lack specific antagonists. Since (1) both propoxyphene and norpropoxyphene possess local anesthetic effects not reversible by specific antagonists and (2) in view of the higher plasma and tissue concentrations of norpropoxyphene attained during chronic propoxyphene administration, as well as (3) the relatively long half-life of norpropoxyphene, questions have been raised regarding the possible role of the local anesthetic properties of the parent compound and its principal metabolite in propoxyphene-induced toxicity.

Compounds possessing local anesthetic activity also modify cardiac conduction. Since electrocardiographic