

Now, concerning the comparisons of propoxyphene with other mild analgesics, first propoxyphene compared to codeine. Since propoxyphene is a "weak" narcotic, oral codeine is the most appropriate standard of comparison.

My review of the literature in 1966 led me to the conclusion that propoxyphene hydrochloride was definitely less potent on a milligram basis than codeine, my best estimate of the relative potency of the two drugs being that propoxyphene is one-half to two-thirds as potent as codeine.

In the interval, no definitive relative potency assay comparing graded doses of the two drugs has appeared, but the results of a few more recent clinical studies are generally consistent with the above estimate.

Two other studies designed to evaluate the analgesic effect of two consecutive doses of each of the study medications, suggest that propoxyphene napsylate 100 milligrams is approximately equianalgesic to codeine 60 milligrams, but deficiencies in data presentation make it impossible for me to judge the validity of this interpretation.

Mr. Chairman, I am leaving out the reference citations which back up all of these statements that I have been making because I assume they will appear in the printed record of my statement.

Senator NELSON. Yes; they will appear in the record.

Dr. BEAVER. Now, propoxyphene compared to aspirin, acetaminophen or APC: The results of studies I reviewed in 1966 and a few more recent studies comparing propoxyphene hydrochloride 65 milligrams or propoxyphene napsylate 100 milligrams with aspirin 650 milligrams, acetaminophen 650 milligrams or 1,000 milligrams, or APC 2 tablets are consistent with the evaluation which I presented to this subcommittee in 1970; namely, that propoxyphene at recommended doses is certainly no more, and probably less, effective than usually used doses of aspirin, acetaminophen or APC.

Concerning the efficacy of propoxyphene as a constituent of drug combinations. Relatively little propoxyphene is used as a single-entity analgesic. Well over 80 percent of the prescriptions for propoxyphene products are for combinations of propoxyphene with acetaminophen, APC, or aspirin.

The rationale for these combinations is the same as that which underlies combinations of codeine and other yet more potent narcotics with these same antipyretic-analgesics; namely, production of more intense analgesia than can be provided by using a single agent and reduction of side effects by reducing the dose of any one analgesic.

Although experimental evidence to substantiate these theoretical rationales is far from ideal or complete, there is a substantial body of evidence from well-controlled clinical analgesic trials to indicate that combinations of appropriately chosen doses of antipyretic-analgesics with narcotics do, in fact, achieve these objectives.

The slopes of the log dose-response curves of analgesic drugs are relatively flat, with the result that even successive doubling of the dose produces only modest increments of analgesic effect.

Narcotics and antipyretic-analgesics such as aspirin are known to produce analgesia by different mechanisms, and the simple additive