Letters

Darvon Safety

Parts of the article, "Federal government faces painful decision on Darvon" by R. Jeffrey Smith (News and Comment, 2 Mar., p. 857) are misleading and not objective. A few remarks may add balance to the discussion.

The impression that Eli Lilly and Company has acted irresponsibly in promoting and discussing Darvon (propoxyphene hydrochloride) with physicians is clearly implied by Smith when he uses words like "Lilly . . . used to claim that . . . ," "physicians remain apparently uninformed of the true nature of the drug . . . ," and the quote that "by not calling Darvon a narcotic, Lilly was not informing physicians about its narcotic properties." These insinuations ignore the fact that pharmaceutical manufacturers must conform to Food and Drug Administration-approved labeling that requires full disclosure of a drug's therapeutic usefulness, limitations, and adverse reactions or side effects. Most of what is known about the pharmacology and metabolism of Darvon has come from research done by our own scientists. The results of their work have been published in scientific journals. Our product labeling and promotional materials have faithfully reflected new information as it has been accumulated.

Lilly has gone beyond the legal requirements. In 1976 our sales representatives contacted more than 100,000 physicians throughout the country to present new warning information that stemmed from the results of a Lilly-sponsored study. This information included warnings that Darvon should be taken only as directed and not in conjunction with alcohol or other central nervous system (CNS) depressants. All manufacturers of propoxyphene are now required to include similar warnings in their package literature. In reporting that Department of Health, Education, and Welfare (HEW) Secretary Califano ordered that warnings be sent to hospitals and physicians, Smith could have pointed out that Lilly's labeling reflected these warnings almost 3 years before.

The fact is that physicians *do* know about the measures required for the safe use of propoxyphene. Eighty-eight percent of the physicians interviewed in a nationwide survey taken earlier this year by an independent market research firm said they are aware of the warnings about the use of propoxyphene alone or in combination with other CNS drugs (including alcohol).

Smith also writes that Lilly once promoted Darvon as "the ideal alternative to codeine." We continue to promote Darvon as "the best available alternative to codeine." Physicians prescribe Darvon because their experience has taught them that, in situations where either codeine or Darvon might be appropriate, patients using Darvon do not experience the side effects that often arise when codeine is prescribed.

The analgesic efficacy of propoxyphene has clearly been established in clinical trials. The National Academy of Sciences–National Research Council's 1969 review (*1*) of propoxyphene affirmed the efficacy of 65-milligram doses of Darvon. Moreover, the previously cited survey of practicing physicians showed that 90 percent of the group found propoxyphene clinically effective in their practice.

William T. Beaver presented a scholarly analysis of the effectiveness and safety of propoxyphene to the Senate subcommittee chaired by Senator Nelson. Smith quotes excerpts not reflecting Beaver's overall position. For example, Beaver's statement that "at recommended doses propoxyphene produces an extremely low incidence of any sort of adverse effect and a virtually zero incidence of serious adverse effects" is not mentioned.

Effectiveness and safety are the two major reasons why billions of doses of Darvon have been prescribed for millions of patients. No amount of salesmanship and promotion could generate the continued sale and use of a drug that did not perform as expected by both the prescribing physician and the patient.

When one keeps in mind the many millions of patients over the past two decades who have safely received relief from pain with Darvon, the reports of dependence are so insignificant that they are nearly unmeasurable. Lilly has received only 402 reports of alleged dependence since 1957. Of the 402 reported cases of addiction, in only 122 was there sufficient evidence to support inference of propoxyphene-induced dependence.

Another significant point missed in Smith's comments came from testimony by Kenneth A. Durrin, director of the Office of Compliance and Regulatory Affairs of the Drug Enforcement Administration (DEA). Durrin questioned whether the data being gathered by DEA would support the criteria provided by law for placing propoxyphene in Schedule II of the Controlled Substances Act.

Eli Lilly and Company is convinced that the objective, full review of the safety and usefulness of Darvon ordered by Secretary Califano on 15 February will confirm that Darvon is a useful analgesic, capable of safely relieving pain.

C. W. PETTINGA
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Reference

1. Analgesic Drugs Panel, *National Academy of Sciences-National Research Council Drug Efficacy Study Investigation Review of Propoxyphene Hydrochloride Compound* (DESI 10996, NDA 10996, Log 27, National Academy of Sciences-National Research Council, Washington, D.C., 1969).

Tea and Tannins

Eliot Marshall's statement (News and Comment, 23 Feb., p. 731) that tea contains more tannic acid than beer is in error. In fact, tea contains *no* tannic acid. Tannic acid is a hydrolyzable tannin that yields on hydrolysis gallic acid and glucose (*1*). It is most commonly described as a pentadigalloyl glucoside with the empirical formula of $C_{76}H_{52}O_{46}$ (*2*). This material has never been reported as a component of tea in any serious work dealing with analysis of the product (*3*). Careful review of the "Federation of American Sciences [sic] for Experimental Biology" report (*4*) referred to by Marshall indicates that tannins are widely distributed in many foods, including tea, but that tannic acid is a more narrowly defined substance. The authors of this report were careful to distinguish the tannic acid under evaluation as a food additive from the tannins that are ubiquitous in plants.

Since Marshall's unreferenced statement is not unique, this "fact" appears to have entered into the domain of common, albeit erroneous, knowledge. When one considers the existing climate surrounding the safety and use of food additives, it is particularly important that what is or is not contained in a food is accurately reported.

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