Benzoyl Peroxide Analysis

In a recent paper[1] in this Journal, "High-Pressure Liquid Chromatographic Assay of Benzoyl Peroxide in Dermatological Gels and Lotions," the authors questioned the validity of a TLC system described by our laboratories in a paper[2] entitled "The Stability of a Benzoyl Peroxide Acne Cream Product." The reliance on removing and measuring spectrophotometrically an extract from the solvent front of a chromatogram was recognized, and a subsequent paper[3], "An Improved TLC Procedure for the Quantitative Determination of Benzoyl Peroxide in Acne Creams," was published. This procedure utilized acetonitrile–water (1:1) in a reversed-phase system on an acetylated support, and complete resolution was achieved with benzoyl peroxide (R_f 0.42), benzoic acid (R_f 0.9–1.0), and other isolable impurities. Excellent assay agreement was obtained between this method and an iodometric titration procedure in deliberately degraded cream formulations. The fact that the iodometric titration procedure was proven to be stability indicating suggests its use as an assay method in terms of economics and simplicity over chromatographic methods.

D. L. Simmons
Research and Development
Frank W. Horner Ltd.
Montreal, Canada H3C 2W6

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[1] F. W. Burton, R. R. Gadde, and W. L. McKenzie, *J. Pharm. Sci.*, **68**, 280 (1979).
[2] D. L. Simmons, H. S. L. Wood, J. J. Liston, and R. J. Ranz, *Can. J. Pharm. Sci.*, **2**, 101 (1967).
[3] D. L. Simmons *et al.*, *ibid.*, **4**, 46 (1969).

Drug Stability in Veterinary Dosage Forms

The January 1979 issue of this Journal contained an editorial on "Consistency in Stability Testing"[1]. This timely editorial was of great interest to the Review Chemists in the Bureau of Veterinary Medicine of the Food and Drug Administration because they are deeply involved in the review and evaluation of stability testing of drug products.

The Bureau of Veterinary Medicine is a counterpart to the Bureau of Drugs, though with a smaller contingent of Review Chemists. The public only hears about veterinary medicine on such issues as DES, nitrites, nitrofurazones, and low-level antibiotics. The Bureau, however, has a much larger responsibility in approving drugs for animal use. Such critical areas as animal safety and human safety must be considered in addition to the effectiveness of the drug. The process of approval is just as intense as that for human products. In many cases, the approval is more critical since food products are involved.

Veterinary drug products are sold as pharmaceutical dosage forms (identical in many cases to the human dosage forms except for labeling), as medicated feed preparations (premixes, supplements, and complete feeds), and as other forms such as medicated blocks.

Bureau Review Chemists are responsible for evaluating the manufacturing operations related to the production of the final products to ensure that they meet the standards they purport to possess.

Stability is an important issue for veterinary products just as it is for human products. In fact, the issue is much more complex because of the variety of products and use patterns. Because of these complexities and often questionable areas of stability testing for veterinary products, the Bureau of Veterinary Medicine developed a set of guidelines for industry and reviewer use. The Bureau issued the Guidelines in July 1976 with a *Federal Register*[2] notice of availability in November of the same year. The Guidelines were updated in February 1978.

For veterinary products, stability is probably more critical and harder to focus on. Because of obvious reasons, human drug products enjoy a much higher plateau in the various fields of research and methods development. Human products are often used under controlled situations or conditions—stored in pharmacies and used in clinics, hospitals, and households. Probably the only controlled conditions for veterinary product usage, however, are in veterinary clinics, hospitals, or offices. Use by farmers of drugs purchased by them or dispensed to them leaves much to be desired as far as stability and shelflife are concerned. Many animal drugs are subjected to higher temperatures and abuse than human drug counterparts. However, as provided under our laws, a veterinary drug is a "drug" and must meet the requirements and individual standards of strength, quality, purity, and identity as proclaimed by the Act. The drug must also be manufactured under the cGMPs as published by the FDA.

We, in the Bureau of Veterinary Medicine, feel the Guidelines we have issued are meaningful and provide the guidance needed by industry. Many companies concerned with human pharmaceuticals are currently using our Guidelines. The Guidelines represent our best scientific judgment on the topic and should be used as just that—"guidelines." Our general position is that every product is unique and must "stand on its own" as far as stability is concerned.

Copies of the drug Guidelines can be obtained by writing to the: Food and Drug Administration, Bureau of Veterinary Medicine, Industry Relations Branch, HFV-226, 5600 Fishers Lane, Rockville, MD 20857.

John R. Markus
Scientific Evaluation
Bureau of Veterinary Medicine
Food and Drug Administration
Rockville, MD 20852

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[1] E. G. Feldmann, *J. Pharm. Sci.*, **68** (1), I (1979).
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Unified Theory of Anesthesia

The current diversity of theories of narcosis indicates a lack of understanding of the mechanism of anesthesia at the molecular level. Ecanow and coworkers[1,2] have proposed a hypothesis that integrates the descriptive, clinical, and laboratory data concerning individuals in a state of anesthesia.

This hypothesis is based on the concept that neuronal cells, like all cells, have membranes in the coacervate state; that is, the membrane exists as an aqueous phase that is in a different thermodynamic state than that of the surrounding aqueous plasma and interstitial fluids[3]. The addition of a small increment of drug to a coacervate phase produces a change in structuring, which results in a free energy change which is chiefly entropic. Accompanying the free energy change are pharmacological changes[1–3].

The colloid theory initially proposed by Claude Bernard in 1875 and subsequently elaborated by others suggested that a reversible aggregation of cell colloids causes or accompanies anesthesia. This reversible aggregation is precisely what occurs upon the introduction of an anesthetic agent to the colloidal system known as the coacervate phase. The change in aggregation relationships is measured by changes in physicochemical properties[3]. These changes, in turn, correlate with the ranking of clinical potencies in a series of depressant drugs[2].

The lipid theory advanced by Meyer and Overton proposes a direct parallelism between the affinity for a lipid phase and its resultant central nervous system (CNS) depressant action. The affinity is