Cyanocobalamin Degradation

In the May 1976 issue of the Journal, Yazdany and Badii[1] reported on the degradation of cyanocobalamin when autoclaved in the presence of 0.1% methylparaben sodium. This observation is not surprising since cyanocobalamin is known to be inactivated in alkaline solutions[2] and methylparaben sodium (a sodium phenolate) gives an alkaline pH in solution. Thus, we are dealing here simply with a base-catalyzed degradation. The authors of the paper seem uncognizant of this and suggest instead some undefined direct interaction between the paraben moiety and cyanocobalamin.

The relatively isolated situation of the authors may explain their unawareness of the nature of the reported reaction. It is surprising, however, that the Journal's reviewer failed to call it to their attention.

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[1] S. Yazdany and F. Badii, *J. Pharm. Sci.*, **65**, 745(1976).
[2] A. Osol, "United States Dispensatory," 27th ed., Lippincott, Philadelphia, Pa., 1973, p. 359.

Equations for Bolus Intravenous Injection in Linear Pharmacokinetics

S. Niazi[1] recently stated that in a linear pharmacokinetic model where instantaneous input is assumed (*i.e.*, bolus intravenous injection), the assumption embodied in Eq. 1 is made:

$$\frac{1 - e^{-b_i\theta}}{b_i\theta} = 1 \qquad \text{(Eq. 1)}$$

He suggested that the coefficients of the bolus intravenous equation should be corrected by multiplying by the reciprocal of the left-hand side of Eq. 1. I would like to caution readers *not* to make such "corrections," since Eq. 1 is incorrect.

The equations for bolus intravenous injection, during a constant rate intravenous infusion, and after constant rate infusion are shown below. They are derived for different initial conditions but are consistent, and the coefficients may be interconverted by means of Eqs. 5 and 6.

For bolus intravenous injection:

$$C_p = \sum_{i=1}^{n} C_i e^{-b_i t} \qquad \text{(Eq. 2)}$$

During an infusion:

$$C_p = \sum_{i=1}^{n} X_i(1 - e^{-b_i t}) = \sum_{i=1}^{n} \frac{C_i}{b_i\theta}(1 - e^{-b_i t}) \qquad \text{(Eq. 3)}$$

After infusion:

$$C_p = \sum_{i=1}^{n} Y_i e^{-b_i t} = \sum_{i=1}^{n} C_i \left(\frac{e^{+b_i\theta} - 1}{b_i\theta}\right) e^{-b_i t} \qquad \text{(Eq. 4)}$$

From Eq. 3:

$$C_i = X_i b_i \theta \qquad \text{(Eq. 5)}$$

From Eq. 4:

$$C_i = \frac{b_i\theta Y_i}{e^{+b_i\theta} - 1} \qquad \text{(Eq. 6)}$$

In Eqs. 1–6, θ is the infusion time, t is time from the start of administration, and the b_i's are eigenvalues. For the two-compartment open model, $n = 2$; for the three-compartment open model, $n = 3$.

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[1] S. Niazi, *J. Pharm. Sci.*, **65**, 750(1976).

Drug Delivery Systems versus *Dosage Forms*

The phrase "drug delivery system" is becoming increasingly prominent in professional communications. It would be well to consider the distinction between this phrase and the classic term "dosage form."

As currently used, a drug delivery system is really a dosage form delivery system. It delivers the physical–chemical system, *i.e.*, the solution or suspension, *etc.*, that contains the drug (*e.g.*, a drug in solution contained within a polymeric matrix). Thus, in the case of Ocusert, the polymeric plastic material contains the solution which is the dosage form and which, in turn, contains the dissolved drug, pilocarpine.

By way of illustrating possible confusion, a capsule that is recognized as a dosage form is really a dosage form delivery system. The gelatin capsule itself can deliver any of a variety of physical–chemical systems (dosage forms) such as suspensions, solutions, or powders. A further illustration exists with intravenous injectables. Here the syringe is the dosage form delivery system; the solution, suspension, *etc.*, are the dosage forms containing the drug.

We suggest that the term "drug delivery system" be used to refer to the dosage form. The pharmaceutical community would do well to consider the confusions that are developing through ill-defined terminology.

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