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Commentary on digoxin bioavailability by Colaizzi

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be subject to recall due to failure to meet the U.S.P. content uniformity test. It was pointed out, therefore, that the low serum digoxin levels produced by these tablets could have been due to low tablet potency rather than poor bioavailability. Although another lot of tablets that showed differences in serum levels when compared with the innovator brand was found to meet all U.S.P. specifications, still other possible criticisms of the Lindenbaum study were noted, such as the use of too few subjects and failure to obtain serum levels over a more prolonged period of time than five hours.

In a more recent publication by Wagner *et al* [5], two brands of digoxin tablets were studied according to an experimental design which suffered from none of the shortcomings of the Lindenbaum *et al* study. The results of this study by Wagner *et al* confirm the implications of the Lindenbaum article that there may indeed be significant differences in bioavailability among different brands of digoxin tablets, even though such tablets may meet all current U.S.P. requirements.

While it now seems likely that significant bioavailability differences among chemically equivalent brands of digoxin tablets pose a distinct concern for the pharmacist, it should also be noted that the two studies cited [2, 5], as well as other recent findings, indicate that there are three other types of bioavailability problems with digoxin: (a) Significant differences in bioavailability may be expected depending upon whether digoxin is administered by the oral or parenteral routes.[5] (b) Significant differences in bioavailability may be expected between oral tablets and oral solutions.[6, 8] (c) Significant variations in bioavailability may be found even among different lots of the same brand of digoxin tablets. The latter variations arise out of formulation changes made by the manufacturer, such as those which caused a doubling of the bioavailability of the innovator's brand of digoxin tablets in England last year.[7, 8]

While the topic of digoxin bioavailability will be treated in somewhat greater detail in the forthcoming Bioavailability Pilot Project report to be published by APhA, the findings summarized above make it apparent that the following points should be given serious consideration by pharmacists at this time:

(1) Therapeutic inequivalence may result from differences in bioavailability between different brands of U.S.P. digoxin tablets.

(2) Different dosage forms (e.g., elixirs vs tablets), even from the same manufacturer, are likely to differ in their respective bioavailability for the same labeled strength, and dosage adjustments may be advisable when transferring a patient from one form to another.

(3) Different lots of the same brands regardless of the manufacturer or source, may not be equally bioavailable and, therefore, they may not be therapeutically equivalent. Consequently, pharmacists might wish to consider recording the lot number of digoxin tablets dispensed as well as the brand.

(4) The evidence, as presented in the study by Wagner *et al*, as well at other studies, documents strongly the need for knowledgeable pharmacist input regarding the choice of manufacturer and in dispensing digoxin products. A pharmacist should not blindly rely on using any brand of digoxin (no matter what the size or reputation of the manufacturer); rather, he should continually seek to request and evaluate data on digoxin tablets from his sources.

It would definitely be in the public interest for the pharmacist to demand—as a condition of purchase—bioavailability data from the suppliers of digoxin tablets, and to be certain that such information is properly and carefully evaluated.

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Published bi-weekly by the American Pharmaceutical Association, 2215 Constitution Ave., N.W., Washington, DC 20037. Donald E. Prescott, Editor. Annual subscription: Members receive the APhA Newsletter every other week as part of their annual membership dues. Second class postage paid at Washington, D.C., and at additional mailing offices.

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