Pharmaceutical Research, Vol. 5, No. 4, 1988

Letter

Approaches to Drug Stability

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Received December 4, 1987; accepted December 4, 1987

KEY WORDS: initial-rate method; decomposition products; stability-indicating assay.

The article "A Critical Appraisal of Drug Stability Testing Methods" [*Pharm. Res* 4:177–180 (1987)] was an attempt to highlight some of the current imperfections in the general approach to drug stability testing which one observes in published reports on this subject.

I apologize for misattributing Dr. Chafetz's review article, but I believe that the term "stability-indicating assay" is very generally taken to mean one which is specific for intact drug (in the presence of its decomposition products) and high-performance liquid chromatography (HPLC) is the single analytical procedure most suitable for this in the majority of stability situations.

In my opinion, the full potential of HPLC in stability is not being exploited. It is most usually applied to assay the undecomposed drug. I suggest that we should also determine drug decomposition products on a quantitative basis and I freely acknowledge that this will require prior characterization of these products. The initial-rate method will then provide information on the rate constants of individual decomposition reactions. This must be an improvement upon the use of rate constants which may be the sum of several individual rate constants and the subsequent use of these to provide some ill-defined activation energy.

I agree wholeheartedly with Dr. Chafetz that extensive stressing applied to drug systems is quite unrealistic and I agree that the effect of additional nonconstant factors such as headspace oxygen should be realized. It is the case, however, that the latter will apply to any stability testing protocol that requires 75% decomposition of a drug, viz., determination of the apparent order of reaction, or even nonisothermal stability testing procedures.

I hope that I did not suggest in our review article that the "so-called initial-rate method" was a panacea for stability ills. It was an attempt to point out that this classical chemical kinetic method, neglected I believe because of the complexity of drug decomposition processes, could, with modern analytical methodology, be used to advantage in appropriate circumstances.

Surely the more information we have about a drug decomposition system, the better? Such information can now be obtained using HPLC and I maintain that, in spite of the complexity of such systems and the limitations of the initial-rate method, a more unified approach should be sought to the study of drug stability and instability.

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