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Short Communication

Replacement of microbiological assays of antibiotics based on high-performance liquid chromatography

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In a recent publication A. H. Thomas [1] examined the replacement of the microbiological assay of antibiotics by an assay based on HPLC. This modification is underway both in the USP and the Ph. Eur. I fully agree with his presentation of the difficulties caused by the USP expression of potency in $\mu g\ mg^{-1}$. In the Ph. Eur. potency is defined in International Units (as defined by W.H.O.) mg^{-1} when using a microbiological assay and the purity is defined as a percentage for a chemical or physicochemical method of assay. The expression of potency in $\mu g\ mg^{-1}$ in the USP and in I.U. mg^{-1} in most other pharmacopoeias leads to a lot of confusion. Unfortunately, harmonization seems unlikely in the near future. For that reason, chemical and physicochemical assays will simplify the problem.

In the Ph. Eur. we already have chemical assays for the penicillins (iodometric assay in the first edition, mercurimetric assay in the second edition), spectrophotometric assays for chloramphenicol and its palmitate, griseofulvin and rifampicin, and gas chromatography for clindamycin and lincomycin. HPLC methods will probably be introduced in 1988 for the assay of daunorubicin and doxycyclin, and for the determination of the components of gentamicin. The next candidates for HPLC methods are several cephalosporins, the tetracyclines and erythromycin. HPLC is being considered for the aminoglycosides, but gentamicin (with four main components) and neomycin (with two main components) will present problems. Complex mixtures such as bacitracin, colistin, nystatin and polymyxin will probably continue to be assayed for a long time by microbiological methods.

As Thomas [1] pointed out, the conversion of the results of HPLC to bioequivalent potencies, as advocated by some authors [2, 3], is not desirable; in fact, it could be considered to be useless. When the microbiological potency of component B is compared with that of component A, the results depend on the micro-organism, the medium used and on the other assay conditions [4], which means that there is no single conversion

factor between the physicochemical method and the bio-assay. Moreover, the micro-organisms used are laboratory bacteria and not the pathogens encountered in clinical practice. The response of a patient to a specified amount of drug will depend on the state of his health and on the nature of the pathogen itself (i.e. virulence, susceptibility or resistance to the antibiotic). Thus a bio-assay should not be expected to give more information than a chemical or a physicochemical determination.

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