PHARMACOPŒIAS AND FORMULARIES

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A Review of the Analysis of Organic Compounds and Pharmaceutical Preparations

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The British Pharmaceutical Codex, 1949, presents many new features compared to the issue of 1934 and its supplements. As an analyst I am pleased to record that most of the drugs have been exactly defined, either by reference to the British Pharmacopœia or by a description on pharmacopœial lines. The B.P.C. has become a book of standards in the same way as the B.P.

Organic Compounds. Nothing revolutionary has been introduced in the tests for identity. These tests seldom give complete identification; no drug is exactly defined until it has passed all the tests. The identifications mainly include qualitative reactions for elements, radicals, etc. Often a characteristic derivative is prepared, isolated, and identified, e.g., by its melting-point or optical activity. Properly, the melting-point or any physical constant of the substance itself should be put under the heading identity, but this is merely a question of convenience. Three of the four barbiturates are chiefly characterised by their melting-points, cyclobarbitone also by the m.pt. of its *p*-nitrobenzyl derivative. As the m.pts. of many of these drugs lie close together it would be advisable to differentiate them, *e.g.*, by derivatives or by titrations, argentometric or bromometric (the allyl compound).

Among the tests for purity the dangerous contaminations with arsenic and lead are traditionally estimated, as are the content of moisture and ash. Also, more quantitative or semi-quantitative determinations of impurities are prescribed than before. But in many cases the tests for purity still are qualitative. Now that the trend in all countries—not least in the U.K.—is to use instruments which permit the estimation of even traces of impurities, is not the time approaching when all pharmacopœias will introduce quantitative methods even for impurities? Such a transition certainly implies much work, but it would be worth while. The control tests for Congo red seem to be insufficient; deaths have followed the injection of impure material.

In this edition assays for organic compounds are more frequently required than formerly. Assays are not included for drugs which are easily defined in other ways—*e.g.*, acetanilide—or which are difficult or impossible to determine. Among the alkaloids—some 20—the titrimetric procedure is required for 10, but the base is extracted and titrated in only half that number, though it is possible in at least 10. Drying of the chloroform extract so frequently directed is unnecessary, even if ammonia is the alkalising agent. Pholedrine sulphate can be easily determined bromimetrically.

The compilers of the Codex have not had the courage to introduce chromatographic methods, which are so convenient for many alkaloidal salts (with Al_2O_3) and salts of metals with inorganic or some organic acids (with cation exchange resins). Nitrobenzene is used to enclose the

AgCl in Volhard titrations, but not consistently. As often as possible a drug is determined by its optical activity.

The photometric or fluorimetric assays are very few, though such methods often are rapid, easy, and specific. Also, it seems feasible to state a value for the molecular or specific extinction at a certain wave-length instead of referring to a standard curve of an auxiliary substance (folic acid). The use of Lovibond units for burnt sugar is certainly practical, but might have been completed by figures more generally applicable. Among the relatively few gravimetric assays in the monographs the determination of methylamphetamine is worth noticing. It is not clear why, when a weighing should be accurate this is always mentioned but never for an accurate measuring (*e.g.*, phenoxyethanol, where the pipetting of the acetic anhydride-pyridine solution is extremely critical).

Formulary. Much work has been done to provide determinations for so many of the preparations. The principle seems to be to provide an assay of the active ingredients of all stored preparations. But when known methods are too inaccurate, or too difficult, none has been included, and the monograph left incomplete. I think this is the way to proceed the first time a new scheme is tried. However, very often no assay is given, though it would have been easy. In the next edition the list of assayed preparations will presumably be longer.

It must be emphasised that the determinations appear to be reliable, especially considering the complex nature of many of the formulæ. Contrary to the Monograph part, many of the quantitative analyses in the Formulary are gravimetric, perhaps in order to give the analyst an opportunity of identifying and testing the ingredient thus isolated. Yet, this is seldom mentioned in the text. The gravimetric procedures are sometimes unnecessarily long and less exact than other methods possible. A typical example is the determination of phenolphthalein in emulsion of liquid paraffin with phenolphthalein, where the weighing of 17 mg. concludes a complicated analysis. Here a photometric estimation can be done, starting with one fortieth of the quantity of emulsion now required. The weights per ml. are stated for all liquid preparations, for tinctures, etc., also the alcohol content. No biological method is described, which no doubt is very sensible. Finally, some notes on special items. The analysis of liniment of methyl salicylate is a real writing desk procedure, impossible to perform. Mercury is assayed by an amalgam method which is very satisfactory, arsenic (in Blauds pills) by distilling $AsCl_3$, a method nowadays abandoned for better ones. Tablets of erythrityl tetranitrate are determined by a simplified colorimetric method, comparing two solutions.

To sum up, in spite of some criticisms, the chemists in the British Empire and all over the world will use the new B.P.C. with confidence. The analytical new look of the issue will, no doubt, be permanent.