Short Communication

ON THE STANDARDISATION OF THYROID B.P.

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The B.P. method for the standardisation of thyroid in terms of thyroxine-iodine is based on the work of Harington and Randall (1929) who claimed that the iodine in combination as thyroxine is related to the biological activity. When applied to the standardisation of tablets the method has given high and variable results; this has been ascribed to the presence of lactose (Doery, 1945) and the B.P. 1958 introduced an acid washing procedure to eliminate the possible interference of this substance when used as excipient. Subsequently this step in the analysis was introduced for official thyroid powder, since most of the commercial products are obtained in too concentrated a form and are suitably diluted with lactose.

In our hands this modification either for commercial thyroid powder or tablets has not given satisfactory results. This was reported to the appropriate committee of the Pharmacopoeia Commission and a critical examination of the procedure was started in an attempt to solve the problem.

Since a large number of determinations was likely, a less laborious method than the sodium carbonate fusion technique for converting organic iodine to iodide was sought. Such a method was found by modifying the flask combustion technique described by Johnson and Vickers (1959) for the determination of iodine in organic compounds. This gives results which are comparable with, but slightly higher than the classical method. Combustion and titration of the liberated iodide by the proposed method can be carried out in 20–30 min., which represents a considerable saving in time over the official method. The detailed procedure for the general analysis is given in the paper referred to above; this has been adapted for use in the presence of a large amount of organic matter by using a 2 litre flask and a sample weight of up to 0·8 g.

The original B.P. 1958 method, with this modification in combustion, was then applied to samples of thyroid before and after the addition of lactose and it was confirmed that the presence of lactose during hydrolysis markedly increases the apparent thyroxine content. We have also shown that a hydrolysis product of lactose itself precipitates under the conditions of the assay and occludes inorganic iodide thus producing a significant effect in the assay of thyroid for "thyroxine-iodine" content. When the acid washing stage of the B.P. Addendum 1960 was then included in some further determinations, it was found that even with thyroid which contained no lactose, the acid wash itself could cause a considerable lowering of "thyroxine-iodine" content. The results obtained are given in Table I although no particular significance can be attached to the magnitude of the loss, since this may vary from occasion to occasion and from operator

to operator. That losses do occur has been substantiated with a second sample of undiluted thyroid.

Hence it is apparent that the determination of "thyroxine-iodine" is not a satisfactory procedure to apply to lactose diluted thyroid and that the modification introduced by the B.P. to improve the assay has not been

TABLE I

THE EFFECT OF ACID-WASHING ON THE DETERMINATION OF "THYROXINE-IODINE" IN UNDILUTED THYROID POWDER

Per cent "thyroxine-iodine"	
Without acid-washing	With acid-washing
0·24	0·21
0·24	0·18
0·24	0·18
	0·21

successful. For standardisation of thyroid the U.S.P. relies upon a determination of total "iodine in thyroid combination". Such a determination would be unaffected by the nature and amount of diluent present. To assess the validity of this, and to compare the results obtained with those from "thyroxine-iodine" determinations, three samples of undiluted thyroid powder from the glands of oxen, pig and sheep respectively were assayed by both chemical and biological methods.

Several biological systems have been described for the assay of thyroidal substances but from our experience the choice of method lies between that

TABLE II

COMPARISON OF CHEMICAL AND BIOLOGICAL STANDARDISATION OF POWDERED THYROID

Sample	Per cent of "thyroxine-iodine"		Total iodine
	Chemical	Biological (P = 0·95 limits of error)	
	Without acid washing	Rat goitre method	
16354	0·11	0·13 (0·09–0·19)	0·22
Oxen	0·13	0·94 (0·75–1·11)	0·36
Pig	0·24	1·16 (0·93–1·46)	0·64
Sheep	0·21	1·23 (1·0–1·5)	0·49

based on the reduction in the asphyxiation time in mice (Smith, Emmens and Parkes, 1947) or that depending on the anti-thiouracil goitre effect in rats (Reineke, Turner, Kohler, Hoover and Beezley, 1945). Although of these the mouse anoxia method has the apparent advantage of being less laborious, less time consuming and calling for less skill, the results from it were more variable in our hands and we prefer the goitre prevention method.

Although it is desirable that a reference standard should simulate as nearly as possible the samples under examination we chose to make our comparisons against thyroxine sodium and thus avoid the difficulty of using a sample of thyroid as an arbitrary standard. In our assays both standard and samples were administered orally.

The biological and chemical results which have been obtained in the examination of ox, pig and sheep thyroid, together with those obtained on a commercial sample of unknown source, are shown in Table II. They illustrate the lack of relation not only between the biological assay figures and thyroxine iodine determined chemically but also between the biological activity and the total iodine.

The three samples of thyroid from oxen, pig and sheep were kindly supplied by Burroughs Wellcome and Co. The results of their own examination of these samples form the basis of a separate publication (Webb, 1961).

References

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