THE STANDARDISATION AND ESTIMATION OF VITAMIN A.

F271.3 G5 044781

Privy Counc

MEDICAL RESEARCH COUNCIL

Reports on Biological Standards

IV.—THE STANDARDISATION AND ESTIMATION OF VITAMIN A

Edited by

E. MARGARET HUME & HARRIETTE CHICK



LONDON
HIS MAJESTY'S STATIONERY OFFICE
1935

MEDICAL RESEARCH COUNCIL

The Most Hon. the Marquess of Linlithgow, P.C., K.T., G (Chairman).

The Rt. Hon. LORD MILDMAY OF FLETE, P.C. (Treasurer).

W. S. Morrison, M.C., K.C., M.P.

Professor E. D. Adrian, M.D., F.R.C.P., F.R.S.

SIR THOMAS LEWIS, C.B.E., M.D., D.Sc., F.R.C.P., F.R.S.

Professor D. P. D. WILKIE, O.B.E., M.D., M.CH., F.R.C.S.

Professor H. S. RAPER, C.B.E., D.Sc., M.B., F.R.S.

Professor A. J. CLARK, M.C., M.D., F.R.C.P., F.R.S.

Professor J. C. G. LEDINGHAM, C.M.G., D.Sc., F.R.C.P., F.R.S.

Professor J. A. RYLE, M.D., F.R.C.P.

Professor Matthew J. Stewart, M.B., F.R.C.P.

EDWARD MELLANBY, M.D., F.R.C.P., F.R.S. (Secretary).

COMMITTEE ON ACCESSORY FOOD FACTORS (VITAMINS)

(Jointly with the Lister Institute of Preventive Medicine)

EDWARD MELLANBY, M.D., D.Sc., F.R.C.P., F.R.S. (Chairman).

Miss Harriette Chick, C.B.E., D.Sc. (Secretary).

Miss K. H. COWARD, D.Sc.

J. M. HAMILL, O.B.E., M.D., D.Sc.

Professor ARTHUR HARDEN, D.Sc., F.R.S.

SIR FREDERICK G. HOPKINS, O.M., D.Sc., F.R.C.P., P.R.S.

Miss E. M. Hume.

Professor R. A. Peters, M.C., M.D., F.R.S.

O. ROSENHEIM, D.Sc., F.R.S.

S. S. ZILVA, D.Sc.

PREFACE

During the last few years much has been done to make it possible to express vitamin potency in exact quantitative terms, by the improvement of methods of biological measurement and by the adoption of agreed standards. This meets the practical need for means of expressing the strength of the highly concentrated preparations of the various vitamins which are now available for therapeutic use, and the similar need in dietetics for means of measuring the vitamin content both of ordinary foods and of preparations in respect of which special claims are made by their manufacturers. The methods have also immediate value in introducing greater accuracy into fundamental research work in the field of nutrition.

The present international agreement on the subject of vitamin standards is the result of two conferences held in London, in 1931 and 1934, under the auspices of the Permanent Standards Commission of the Health Organisation of the League of Nations. The decisions then taken had been made possible only by a great deal of preparatory research work, very much of which was done in this country. It is of a section of that work, concerned in particular with vitamin A, that the following report gives an account.

At the first International Conference for the Standardisation of Vitamins, in 1931, a provisional unit of vitamin A was established in terms of the biological activity of a sample of carotene. It was necessary to make this standard provisional, in the then imperfect state of knowledge, as it seemed clear that experience would reveal possibilities of improvement. This was soon shewn to be the case. for immediately after the conference several isomeric forms of carotene, including β -carotene, were isolated by various investigators; and, since it was evident that the standard carotene was a mixture, it at once seemed probable that a sample of a uniform substance could be substituted with advantage at some future date. A further point was that the crystalline form of the provisional standard had been found by some workers to be difficult to manipulate, making it desirable that any future standard should be issued The second International Conference, in 1934, accordingly adopted a solution of pure β -carotene as the permanent standard in terms of which units of vitamin A were in future to be expressed.

Much of the preparatory research work on the standardisation of vitamin A, for both the International Conferences, was done by the members of a special sub-committee of the Accessory Food Factors Committee, appointed jointly by the Medical Research Council and the Lister Institute. In the course of this excellent team work all kinds of problems presented themselves, such as finding the best

MEDICAL RESEARCH COUNCIL

The Most Hon. the Marquess of Linlithgow, P.C., K.T., G.C.I.E. (Chairman).

The Rt. Hon. LORD MILDMAY OF FLETE, P.C. (Treasurer).

W. S. MORRISON, M.C., K.C., M.P.

Professor E. D. Adrian, M.D., F.R.C.P., F.R.S.

SIR THOMAS LEWIS, C.B.E., M.D., D.Sc., F.R.C.P., F.R.S.

Professor D. P. D. WILKIE, O.B.E., M.D., M.CH., F.R.C.S.

Professor H. S. RAPER, C.B.E., D.Sc., M.B., F.R.S.

Professor A. J. CLARK, M.C., M.D., F.R.C.P., F.R.S.

Professor J. C. G. LEDINGHAM, C.M.G., D.Sc., F.R.C.P., F.R.S.

Professor J. A. Ryle, M.D., F.R.C.P.

Professor Matthew J. Stewart, M.B., F.R.C.P.

EDWARD MELLANBY, M.D., F.R.C.P., F.R.S. (Secretary).

COMMITTEE ON ACCESSORY FOOD FACTORS (VITAMINS)

(Jointly with the Lister Institute of Preventive Medicine)

EDWARD MELLANBY, M.D., D.Sc., F.R.C.P., F.R.S. (Chairman).

Miss Harriette Chick, C.B.E., D.Sc. (Secretary).

Miss K. H. Coward, D.Sc.

J. M. HAMILL, O.B.E., M.D., D.Sc.

Professor ARTHUR HARDEN, D.Sc., F.R.S.

SIR FREDERICK G. HOPKINS, O.M., D.Sc., F.R.C.P., P.R.S.

Miss E. M. Hume.

Professor R. A. Peters, M.C., M.D., F.R.S.

O. ROSENHEIM, D.Sc., F.R.S.

S. S. ZILVA, D.Sc.

PREFACE

During the last few years much has been done to make it possible to express vitamin potency in exact quantitative terms, by the improvement of methods of biological measurement and by the adoption of agreed standards. This meets the practical need for means of expressing the strength of the highly concentrated preparations of the various vitamins which are now available for therapeutic use, and the similar need in dietetics for means of measuring the vitamin content both of ordinary foods and of preparations in respect of which special claims are made by their manufacturers. The methods have also immediate value in introducing greater accuracy into fundamental research work in the field of nutrition.

The present international agreement on the subject of vitamin standards is the result of two conferences held in London, in 1931 and 1934, under the auspices of the Permanent Standards Commission of the Health Organisation of the League of Nations. The decisions then taken had been made possible only by a great deal of preparatory research work, very much of which was done in this country. It is of a section of that work, concerned in particular with vitamin A, that the following report gives an account.

At the first International Conference for the Standardisation of Vitamins, in 1931, a provisional unit of vitamin A was established in terms of the biological activity of a sample of carotene. It was necessary to make this standard provisional, in the then imperfect state of knowledge, as it seemed clear that experience would reveal possibilities of improvement. This was soon shewn to be the case, for immediately after the conference several isomeric forms of carotene, including β -carotene, were isolated by various investigators; and, since it was evident that the standard carotene was a mixture, it at once seemed probable that a sample of a uniform substance could be substituted with advantage at some future date. A further point was that the crystalline form of the provisional standard had been found by some workers to be difficult to manipulate, making it desirable that any future standard should be issued The second International Conference, in 1934, accordingly adopted a solution of pure β -carotene as the permanent standard in terms of which units of vitamin A were in future to be expressed.

Much of the preparatory research work on the standardisation of vitamin A, for both the International Conferences, was done by the members of a special sub-committee of the Accessory Food Factors Committee, appointed jointly by the Medical Research Council and the Lister Institute. In the course of this excellent team work all kinds of problems presented themselves, such as finding the best

solvent for carotene and determining the conditions under which this substance remained stable in solution. In addition, completely new aspects of the subject arose, including the possibility of measuring vitamin A by a physical method, based on spectrophotometry, which necessitated a comparison of the spectrophotometric results with those obtained by biological methods. Thus researches were made which, although each separate item was possibly of minor importance, became in the mass of great interest to workers in the field. Some of the work had been published by the individuals concerned, but much remained unpublished: it was thought, therefore, that the collection and publication of all the investigations together would constitute an important record, very useful to other experts.

It should be clearly understood, however, that this publication is not to be regarded either as a comprehensive account of the quantitative estimation of vitamin A, or as a detailed guide to the methods of making the tests. It is actually a collection of technical information, not available elsewhere, concerning the properties and use of the international vitamin A standard, and is intended for the information of competent workers already practised in the usual methods for the quantitative estimation of the vitamin.

As in all problems of active and growing importance, it will be seen that in some respects the present account is incomplete and indeed raises fresh problems of great interest. Further work, for instance, is needed to show whether the spectroscopic method of estimating vitamin A is trustworthy, and to establish more precisely the conversion factor relating this method to the results of the biological tests. It is hoped that in this and other ways the present report will stimulate further investigation.

In issuing this report, an instructive example of associated researches directed to a common object, the Medical Research Council would thank all those who have combined in its production, namely, Dr. Katharine Coward, Mr. M. Evers, Miss E. M. Hume, Mrs. K. Lathbury, Dr. I. Smedley MacLean, Dr. R. J. Macwalter, Dr. T. Moore, Dr. R. A. Morton, Dr. O. Rosenheim, and the late Dr. R. S. Morgan. To Miss Hume and Dr. Harriette Chick has fallen the task of co-ordinating and editing all the results of the investigations, and to them also the Council would wish to express their appreciation.

MEDICAL RESEARCH COUNCIL, 38, Old Queen Street, Westminster, S.W.1.