PHARMACOPŒIAS AND FORMULARIES

ADDENDUM 1955 TO THE BRITISH PHARMACOPŒIA 1953*

REVIEWED BY G. E. FOSTER

Rapid advances in medicine and pharmacy have encouraged the General Medical Council to take advantage of that section of the Medical Act, 1950, empowering the Council to publish, between editions of the British Pharmacopœia, amendments to the current edition. To fulfil this purpose the Council has caused to be published the Addendum, 1955, to the B.P. 1953, Besides monographs on new official drugs and their preparations, the Addendum includes monographs on tablets prepared from drugs already official. Opportunity has also been taken to amend existing monographs, where necessary, in order to bring them in line with the most recent knowledge and to correct some minor errors which appeared in the 1953 edition. Of the drugs now afforded official status by inclusion in the Addendum the reviewer was impressed by the number, which had previously been described in editions of the British Pharmaceutical Codex.

The following new drugs are included in the Addendum:—

Carbimazole*
Chloroquine Phosphate*
Chloroquine Sulphate*
Corticotrophin†
Cortisone Acetate*†
Dextran Sulphate†
Diethylcarbamazine Citrate*
Ferrous Gluconate*
Gallamine Triethiodide†
Hexamethonium Tartrate*†
Insulin Zinc Suspension
Insulin Zinc Suspension (Crystalline)
Insulin Zinc Suspension (Amorphous)
Iopanoic Acid*
Isoniazid*
Lignocaine Hydrochloride†
Mersalyl Acid†
Methylamphetamine Hydrochloride*†
Nalorphine Hydrobromide†
Oxytetracycline Dihydrate*
Oxytetracycline Hydrochloride
Phenindione*
Phenylbutazone
Primidone*
Suxamethonium Chloride†

* = Tablets included; † = Injection included

Monographs are also given for tablets of Amphetamine Sulphate, Carbarsone, Di-iodohydroxyquinoline, Hyoscine Hydrobromide, Morphine Sulphate, Pentobarbitone Sodium, Quinidine Sulphate and Soluble Aspirin.

The new drugs cover a broad field of therapeutic agents, the greatest number of additions being in the hormone category. Corticotrophin (ACTH) and Cortisone Acetate both find places, while Insulin Zinc Suspension (I.Z.S.), I.Z.S. (amorphous) and I.Z.S. (crystalline) are all included. It may cause some surprise that Isophane Insulin has been omitted particularly as it has been described in the U.S.P. XV. A requirement for glycerin content has been added to the monographs on Insulin Injection, Protamine Zinc Insulin Injection and Globin Zinc Insulin Injection.

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Of the amendments the inclusion of Purified Water to replace Distilled Water is notable and reflects the increasing use in pharmacy of demineralised water, prepared from potable water by treatment with ion exchange materials. The standard for this type of water, which may also be prepared by distillation, is the same as that previously applicable to Distilled Water with the addition of requirements for pH and albuminoid ammonia content. It will be surprising if the former requirement does not cause trouble, for it is difficult to determine the pH of an unbuffered product like distilled water and on this account one might have expected the B.P. to give specific directions for carrying out the determination. The formulæ of Syrup of Lemon, Syrup of Orange and Calamine Lotion have been amended in order to provide improved preparations.

The attention given to drugs of poor keeping properties is indicated by additional storage conditions. In the case of insulin preparations the statement that they should not be exposed to temperatures exceeding 20° C. has been deleted; the preparations are directed to be kept at as low a temperature as possible above their freezing points. Tablets of Glyceryl Trinitrate and Capsules of Halibut Liver Oil are to be labelled with their date of manufacture and these products are expected to retain their potencies for one and three years respectively when stored as directed by the B.P. The latter statement will create difficulties as pharmacists will naturally consider any stock, after storage for the period indicated, to be unfit for sale. No fault can be found with the B.P. in cases where a product is known to be unstable and an appropriate 'life' has been generally accepted, but when it is known that some manufacturers have carried out research to produce preparations of improved keeping properties it would seem fairer to require that the label should indicate a period during which the product might be expected to retain its potency and to leave each manufacturer to give a 'life' to his own product.

By describing official analytical methods and reagents a new pharmacopœia gives a good indication of advances in pharmaceutical analysis. The Addendum 1955 employs an interesting determination of zinc in the different types of Insulin Zinc Suspension and for this purpose makes use of an extraction titration using a solution of diphenylthiocarbazone in chloroform as reagent. This extraction technique has wide application and is not so well known as it deserves. In view of the established usefulness of titrations of organic bases and their salts in glacial acetic acid with standard perchloric acid solutions, it might have been expected that the Addendum would have found some use for this analytical tool. Both the B.P.C. 1954 and the U.S.P. XV use non-aqueous titrations in appropriate cases and it can only be a matter of time before the B.P. follows their example. The disintegration test for tablets, originally included in the 7th Addendum to the B.P. 1932 and official in subsequent editions of the B.P., has been replaced by a test, similar in principle to that described by Prance, Stephenson and Taylor (*Quart. J. Pharm. Pharmacol.*, 1946, **19**, 286) in a paper presented to the 1946 British Pharmaceutical Conference. There is no doubt that the new test has many advantages over the old.

The importance of biological assays is again emphasised by the inclusion of sections dealing with assays of antibiotics, serological and bacteriological products, hormones and Dextran Sulphate. The test for retardation of insulin effect for Injection of Protamine Zinc Insulin has been amended to allow guinea-pigs as well as rabbits to be used as experimental animals. The fact that it is usual to take the blood sample from the heart rather than from the ear vein in the case of guinea-pigs (Stewart and Smart, *J. Pharm. Pharmacol.*, 1953, **5**, 939) appears to have been overlooked, and it is not made sufficiently clear that the guinea-pig may also be used for the testing of I.Z.S. preparations. The test for pyrogens has been rewritten and now takes the form of a sequential sampling technique designed to use a minimum number of rabbits.

The publication of this Addendum will reassure any who may have feared that the B.P. is not keeping abreast of the most recent advances in medicine and pharmacy. The work has been well produced and proof reading has been well done the reviewer noticing no typographical errors.

The Addendum becomes official from March 1, 1956.

(ABSTRACTS—*continued from page* 66)

injected intravenously into rabbits in doses of 1·4 to 9·9 mg., did not induce pyrogenic activity in the serum. The pyrogenic euglobin of rabbit serum, produced by the intravenous injection of bacterial pyrogens, when injected intravenously into a second rabbit, also failed to induce pyrogenic activity in the recipient rabbit's serum. When injected into dogs, the pyrogenic euglobulin of rabbit serum produced a rise in temperature, and also an initial leucocytosis and a subsequent leucopænia, and the same effects were produced by the alpha-globulin from the rabbit serum. The results suggest that pyrexin from inflammatory exudates and pyrogenic euglobulin formed in the circulatory blood by interaction of bacterial pyrogens are essentially similar in nature. H. T. B.

Pyrogens in the Production of Fever. E. Atkins and W. B. Wood. (*J. exp. Med.*, 1955, **101**, 519.) The rate of clearance of intravenously injected typhoid vaccine was studied in unsensitized, sensitized and pyrogen-tolerant rabbits by means of a passive transfer technique. The blood of unsensitized rabbits which had not previously been exposed to bacterial pyrogen remained pyrogenic for normal recipients throughout a period of 2 hours following the injection. In contrast, rabbits sensitized by having received either one or two injections of the vaccine at least 3 weeks prior to the experiment cleared their blood of the test vaccine within 30 minutes despite the fact that they exhibited the same febrile response as unsensitized rabbits. After 1 hour, however, a transferable pyrogenic substance was again demonstrable in the sera of this group. It is thought that this newly appearing substance may be of endogenous origin and may be the factor which directly affects the thermoregulatory centres of the brain. Rabbits made tolerant by repeated daily injections of vaccine have a characteristically depressed febrile response. Not only were the blood streams of such animals cleared of the injected vaccine within less than 5 minutes but samples of their sera obtained 1 and 2 hours after the injection also failed to contain demonstrable quantities of the secondary pyrogen observed in sensitized animals. The latter observation is in keeping with the suggestion that the secondary pyrogen may play a critical role in the production of fever. S. L. W.

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