General Medical Council

PHARMACOPOEIA COMMISSION

REPORTS OF SUB-COMMITTEES*

In addition to the Reports of the Pharmaceutical Chemistry Sub-Committee and of the Cod-liver Oil Colour Test Sub-Committee (*cf.* ANALYST, **1931**, **56**, **457**), the following Reports have been issued:

* The Reports may be obtained from the General Medical Council, 44, Hallam Street, London, W.1. Prices: No. 1, 1s.; Nos. 2 and 3 together, 3s.; No. 4, 1s. 6d.; No. 5, 1s.; No. 6, 1s. 6d.; No. 7, 1s.; No. 8, 1s. 6d. Criticism of the recommendations is invited.

REPORT OF PHARMACY SUB-COMMITTEE, AUGUST, 1930. (No. 1.)

This Sub-Committee suggests new formulae for certain preparations to be added to the Pharmacopoeia, and makes recommendations relating to the manufacture of some which require alteration. The subjects dealt with include Acids, Alcohol, Confections, Effervescing Preparations, Extracts and Liquid Extracts, Glycerins, Infusions, Liniments, Lozenges, Mucilages, Ointments, Oxymels, Plasters, Powders, Resins, Solutions, Spirits, Suppositories, Syrups, Vinegars, Waters (Aromatic), and Miscellaneous Preparations. The Sub-Committee recommends that Industrial Methylated Spirit should be described in the Pharmacopoeia, and that, subject to the statutory regulations, its use in making solid extracts and certain other preparations should be permitted.

REPORT OF THE SUB-COMMITTEE ON DIGITALIS AND STROPHANTHUS, MAY, 1931. (No. 4.)

The Sub-Committee makes recommendations for the preparation of tincture and infusion of digitalis and of tincture of strophanthus, and puts forward proposals for the biological standardisation of these drugs. Comment is invited on these proposals.

REPORT OF THE SUB-COMMITTEE ON THE PREPARATION OF STERILE SOLUTIONS FOR INJECTION, 4TH MAY, 1931. (No. 5.)

The Sub-Committee was appointed to prepare for the Commission a general statement of the principles to be adopted in sterilising solutions, and to supply notes on the best methods of sterilising the solutions of special drugs, which could be appended to the monographs on these drugs in the Pharmacopoeia. The recommendations cover the sterilisation of glass vessels and containers, heating in an autoclave, Tyndallisation, filtration, sterilisation of oily solutions, and an emergency method of sterilisation. The methods most suitable for certain specific drugs are given. The report deals also with the preparation of sterilised distilled water and of physiological saline solution.

SECOND REPORT OF PHARMACY SUB-COMMITTEE, MAY, 1931. (No. 6.)

This Report presents a résumé of the Sub-Committee's recommendations on the preparation of the following articles for inclusion in the new Pharmacopoeia:—Collodion, Elixir Cascarae Sagradae, Liquid Extract of Liver, Dry Extract of Liver, Dry Extract of Hyoscyamus, Eye Ointments, Hydrargyrum *cum* Creta, Concentrated Infusions, Injections, Liniments, Oxymels, Pills, Powders (for which a system of description based on coarseness or fineness is proposed), Solutions, Spirit of Nitrous Ether, Suppositories, Syrups, and Tincture of Stramonium.

REPORT OF SUB-COMMITTEE ON AMPOULE GLASS, JUNE, 1931. (No. 7.)

Glass containers of medicinal solutions should yield but little alkali to the solutions contained in them, and two tests are recommended for determining the limit of alkalinity. (1) *Applied to the glass when crushed.*—The apparatus to be used is first tested by placing the test solution (100 ml. of water, 0·4 ml. of 0·01 *N* hydrochloric acid, and 0·4 ml. of a strong solution of methyl red, made by dissolving 0·04 grm. of methyl red in 50 ml. of 95 per cent. alcohol, adding 1·5 ml. of 0·05 *N* sodium hydroxide solution and water to 100 ml.) in a vessel of resistant glass, transferring the solution, while boiling, to a 250 c.c. conical flask of resistant glass fitted with a reflux condenser, or with a simple condensing apparatus made by fitting a short wide tube of resistant glass (closed at one end and supplied with a flow of cold water) into the stopper of the conical flask. The whole is placed in a boiling water-bath, and at the end of 1 hour the red colour of the test solution should remain unaltered; otherwise, the flask and condenser are unsuitable for the test. Five grms. of the ground glass (particles passing a No. 25,

but not a No. 36 sieve) are washed free from dust with 95 per cent. alcohol in a small conical flask, and dried at 100° C., and 100 ml. of fresh test solution are added, the condenser is inserted and the contents of the flask are boiled for half-an-hour, when the colour should not have changed from pink to the full yellow of methyl red, as indicated by comparison with a solution prepared by adding to 10 ml. of the test solution 0·1 ml. of 0·1 *N* sodium hydroxide. (2) *Ampoules.*—Not less than 6 ampoules are filled to their prescribed capacity with acid solution of methyl red (8·3 ml. of 0·02 *N* hydrochloric acid and 20 ml. of strong solution of methyl red as above, made up to 1000 ml.) sealed and heated in steam at a pressure of 15 lbs. per sq. in. for half-an-hour. After cooling, the pink colour should show no change on comparison as described above. The tests should, if possible, be carried out not more than 14 days before the ampoule is to be used, and, if stored ampoules do not respond to the test, they should be re-tested after washing internally with a 5 per cent. (v/v) solution of acetic acid, followed by 3 washings with water, provided that, if the ampoules then pass the test, this washing is carried out before they are brought into use.

D. G. H.

REPORT OF SUB-COMMITTEE ON ERGOT, OCTOBER, 1931. (No. 8.)

The conclusions reached by the Sub-Committee are that ergotoxine is to be regarded as the active principle for which ergot preparations are administered; that the colorimetric method carried out as recommended permits of an accurate determation of total alkaloid in ergot, and its liquid extract; that the colorimetric method has advantages over gravimetric methods in requiring smaller amounts of material and less time; and that the margin of error in biological methods is at least as great as that due to the variation in the relative proportion of ergotóxine and ergotinine in the total alkaloid. Since the variation in the alkaloidal content of ergot of rye is wide, the standard for the alkaloid in the liquid extract is important, and it is recommended that it should be 0·05 per cent. of total alkaloid ±0·01. The strength of the official extract is recommended as corresponding with 0·03 per cent. of ergotoxine, and, since the evidence before the Sub-Committee suggests that 60 to 70 per cent. of the total alkaloid consists of ergotoxine, this percentage is equivalent to a total alkaloid percentage of 0·05, measured by the colour test. The M. I. Smith colour test for ergot is capable, particularly in its slightly modified form, of giving results which agree closely in the hands of different workers. The ether must be free from peroxide; and, although hydrochloric acid may be used instead of sulphuric acid, traces of peroxide affect the test to a greater extent, and the sulphuric acid method is recommended for official adoption.

Sulphuric Acid Method.—Five grms. of ergot, in No. 60 powder, are extracted with cold petroleum spirit (b.pt. 40–50° C.), and, when the fat is completely removed, the extracted drug is dried at a temperature not exceeding 30° C., and 100 ml. of anaesthetic ether are added. After standing in a stoppered glass for 10 minutes, 0·5 grm. of light magnesium oxide, diffused in 20 ml. of water, is added, and the mixture is shaken at intervals during 30 minutes. Powdered tragacanth (1·5 grm.) is then put in, and, after shaking, 50 ml. (2·5 grms. of drug) are filtered through cotton wool, and shaken in a separator with 4 successive 10-ml. portions of a 1 per cent. (w/v) solution of tartaric acid in water. The aqueous liquids are separated and mixed, the dissolved ether is evaporated, and water is added to suitable volume (say, 40 ml.), and to 2 ml. of this solution is added with constant shaking, and drop by drop, with cooling arrangements, 1 ml. of a solution of dimethylamino-benzaldehyde (0·25 per cent., w/v, in sulphuric acid). The mixture is exposed to bright light until the blue-violet coloration reaches a maximum. A standard for comparison is made at the same time and in the same way by adding to 2 ml. of a freshly-prepared 0·006 per cent. (w/v) solution of ergotoxine ethane sulphonate in 1 per cent., w/v, tartaric acid, 1 ml. of solution

of dimethyl-amino-benzaldehyde. Quantities are so arranged that the acid solution of alkaloids is diluted to produce a colour very close to that of the standard. The proportional intensities allow of the calculation of the amount of alkaloid. If the liquid extract of ergot is to be assayed, 5 ml. are treated with 50 ml. of water, rendered slightly alkaline with ammonia, and extracted with 40, 25, 20 and 10 ml., successively, of anaesthetic ether, the united extracts are washed with 25 ml. of water mixed with 0·2 ml. of dilute ammonia and then with 25 ml. of water, and the treatment with tartaric acid is carried out as above.

The Hydrochloric Acid Method.—This needs no precautions as to heat. To 5 ml. of liquid extract are added 20 ml. of a 1 per cent. (w./v.) solution of sodium bicarbonate (the mixture should be alkaline to litmus), and the mixture is extracted with 40, 25 and 15 ml. of anaesthetic ether. The united extracts are washed with 10 ml. of a 1 per cent. solution of sodium bicarbonate, and the ethereal solution is extracted with 15 ml. of a 1 per cent. (w/v) solution of tartaric acid. The acid layer is drawn off, and the extraction is repeated twice with 10 ml. of acid. The dissolved ether is removed from the united acid liquids, which are made up to a suitable volume, and the colour test is applied as before, the hydrochloric acid reagent being used.

D. G. H.