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COMMENTS PERTINENT TO THE COMING REVISIONS OF THE U. S. P. AND N. F.*

BY GEORGE E. ÉWE.

Since revision of the U. S. P. and N. F. will shortly be conducted, comments and criticisms which may be helpful in the revision processes are pertinent at this time.

It seems the duty of those having occasion to consult these reference books in their daily work, and who consequently are in a position to judge the practical nature of their contents, to comment upon and criticize certain features in a constructive sense.

Consequently, the following comments are offered with the hope that out of all the chaff sufficient grains may be salvaged to reward the efforts of the winnower.

Aloe, U. S. P.—If the U. S. P. test for "gum or inorganic impurities" is of significance it should be placed on a quantitative basis. Practically no market product will yield a "nearly clear" solution in this test.

Aloin, U. S. P.—It is often difficult to dissolve 1 Gm. in 120 cc. distilled water at 25° C. by shaking frequently during 2 hours and high results are sometimes obtained, as a consequence, for proportion of insoluble matter. A slightly elevated temperature makes this test convenient and reliable. The effect of elevated temperature upon the permissible limit of insoluble matter requires investigation, with the view of making results of this test more certain.

Chloramine, U. S. P.—Caution against contact of this substance with organic materials at elevated temperature might be included as it may cause a conflagration if dampened and then dried on paper in a tablet granulation drier.

Cod Liver Oil, U. S. P.—Vitamin A standard is too low. A method of determining vitamin D should be added.

Compound Resorcin Ointment, N. F.—Usually discolors in a few weeks to a few months and becomes unsightly. Means of preventing this deserve study.

Elixir Four Chlorides, N. F.—Precipitates a mixture of organic matter and mercurous

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* Scientific Section, A. PH. A., Baltimore meeting, 1930.

salts after some months. No particular ingredient is alone responsible as practically each ingredient, with the exception of the hydrochloric acid, will precipitate the mercury salt in time when tried out separately. The alcohol is particularly active in this respect and also the flavoring oils. The only practical method found of largely overcoming this defect seems to be to make a radical change in this product, making it a syrup flavored with methyl salicylate, since sugar and methyl salicylate seem to cause practically no reduction of the mercury salt and a product so made develops only a barely perceptible precipitate in somewhat less than a year. However, this syrup entirely differs from the N. F. elixir in all physical characteristics.

Elixir Glycerophosphates Comp., N. F.—Develops a small but unsightly precipitate after a few months. This defect can be largely overcome by increasing the lactic acid and completely corrected if phosphoric acid is used instead. However, in the latter case the product is practically colorless, whereas the N. F. product is yellowish.

Fluidextract Buchu, U. S. P.—To obtain uniformity in color of succeeding batches and assure brightness of green color the use of Type Process C (fractional or divided percolation) is preferable to Type Process A now prescribed.

Fluidextract Ergot, U. S. P.—A means of stabilizing the activity is needed.

Fluidextract Ipecac, U. S. P.—Often causes cloudiness in Syrup Ipecac made from it. This defect can usually be overcome by using a mixture of 4 or 5 volumes of alcohol to one volume of water along with hydrochloric acid as menstruum throughout; evaporating the extra percolate at not above 65° C. and stopping the evaporation before the concentrated percolate gets excessively cloudy; and insuring clarity of Fluidextract before using it for making Syrup Ipecac by careful filtration aided by a trifle of kieselguhr.

Fluidextract Licorice, U. S. P.—The taste of a product containing ammonia water is preferred. However, the ammonia is preferably not used in percolating but added to the completed product just before filtration.

Fowler's Solution, U. S. P.—Methods of retarding oxidation require study. An assay for total arsenic should be added to establish original strength possessed by the solution before oxidation set in.

Hexamethylenamine U. S. P.—Methyl red as indicator gives sharper end-point in titration.

Hydrastis, U. S. P., and Tincture and Extract Hydrastis, N. F.—The weighed alkaloidal residue obtained in the assay should be corrected for acid-insoluble matters as in the case of colchicum seed.

Hypophosphorous Acid, U. S. P.—Invariably Calcium is present in the market supplies; the average of several lots was 1.42% calculated as calcium hypophosphite. A limit might be established, or at least the presence of calcium declared, as a guard against incompatibility in pharmaceutical work.

Hypophosphites of the N. F.—The alkali specified to effect neutralization after oxidation with nitric acid during the assay process is "Sodium Hydroxide Test Solution (free from Chloride)" in the case of ammonium, calcium, and manganese hypophosphites; "Special Sodium Hydroxide Test Solution (free from Chloride)" in the case of Potassium Hypophosphite and "Special Potassium Hydroxide Test Solution (see Reagents, U. S. P.)" in the case of Sodium Hypophosphite. Uniformity is needed in this respect.

In the assay of Calcium Hypophosphite instructions are given to reject the first 20 cc. of filtrate before collecting the 50 cc. for titration; whereas, in the assay of Potassium and Sodium Hypophosphites the first 25 cc. of filtrate is to be rejected and in the assays for the ammonium and manganese salts no rejection of first filtrate is directed. Consistent instructions are needed in this respect.

In the assay of the Hypophosphites of Ammonium, Calcium, Potassium and Sodium the following less tedious and less laborious process might be permitted as an alternate method: Dissolve 3.5 Gm. of the hypophosphite, previously dried over sulphuric acid for 24 hours, in 1000 cc. water; place 10 cc. aliquot in a glass-stoppered flask, add 35 cc. tenth-normal Potass. Permanganate, 20 cc. water and 1.1 cc. Concentrated Sulphuric Acid; shake, stopper and let stand for 24 hours in the dark; add 5 cc. Potassium Iodide T. S. and titrate with tenth-normal Thiosulphate. Make correction for blank.

One cc. tenth-normal Permanganate is equal to 0.002075 Gm. Anhydrous Ammonium Hypophosphite; or 0.002125 Gm. Anhydrous Calcium Hypophosphite, or 0.002601 Gm. Anhydrous Potassium Hypophosphite, or 0.002648 Gm. Sodium Hypophosphite containing 1 molecule of water.

Lithium Benzoate and Lithium Salicylate, N. F.—A more distinctive assay process is advisable, such as separation of, followed by titration of, the acid radical.

Mercuric Iodide, U. S. P.—A more available assay method is advisable. The iodate titration method is eminently satisfactory; or precipitation as sulphide after solution of the iodide in either potassium iodide or sodium thiosulphate solutions can be used.

Oil Birch Tar, Rectified, N. F.—Warning might be included against storage in tinned iron containers (the common method at present), which soon blackens the oil with the result that the color of products in which the oil is used is spoiled.

Ointment Boric Acid.—A product made with white petrolatum is more elegant and is preferred by the "trade" and should be adopted if not unwarranted by therapeutic considerations.

Ointment Sulphur, U. S. P.—Pharmaceutical elegance dictates the use of petrolatum or a mixture of petrolatum and anhydrous lanolin as base if therapeutic considerations do not forbid.

Proximate Assays, U. S. P.—Under "evaporation of solvents" (page 453): In addition to the alkaloids of Hyoscyamus, the alkaloids of Ipecac could be stated as being sensitive to heat. Since the object of this passage appears to be a warning against the overheating of certain alkaloidal residues it might be well to direct that the solution of alkaloids in volatile solvent be not entirely evaporated to dryness with heat and that the last several cc. be evaporated with a current of dry air at room temperature.

It might be well to state that no visible water should be present during the evaporation of solvents containing hydrolyzable free alkaloids, such as those of the mydriatic drugs.

It is not necessary to treat alkaloidal residues obtained from Chloroform with ether or alcohol when the residue is to be titrated but this procedure is advisable when the residue is to be weighed.

It would also be well to direct that alkaloids obtained in gravimetric determinations be corrected for acid-insoluble matters somewhat like the directions under Colchicum Corm and Seed.

Sodium Nitrite, U. S. P.—If present assay process is retained some such modification as follows is desirable: Add the Oxalic Acid Solution one cc. at a time, shaking well after each addition until the liquid becomes absolutely clear and colorless (there will be an excess of oxalic acid at this stage); then titrate back slowly with Permanganate Solution.

Soft Soap, U. S. P.—When made without added glycerin was clearer than with glycerin, even after one and one-quarter years. If glycerin can be deleted cost of production can be reduced. This suggestion is based upon a single observation and requires confirmation by other observers.

Solution Acid Phosphates, N. F.—Trouble has been experienced with fungous growths. These have been prevented by the addition of about 1% of concentrated hydrochloric acid along with 0.4% of formic acid.

Spirit of Nitroglycerin, U. S. P.—A more distinctive assay process is preferable, such as the Devarda Alloy method.

Strontium Salicylate, U. S. P.—Is usually quite acid, due to excess of salicylic acid. One lot had acidity to phenolphthalein corresponding to 0.73% free salicylic acid. The U. S. P. prescribes no reaction test at present. A limit of acidity should be stated. Also a more distinctive assay process is desirable, such as separation of the salicylic acid with subsequent titration.

Sulphur, Sublimed, U. S. P.—Fifty cc. of a 1 to 10 solution of Potassium Hydroxide is prescribed for dissolving the 1 Gm. sample at boiling temperature. This concentration is too weak and solution is unduly delayed which results in loading the solution with silica when the process is conducted in glass. A 1 to 2 solution of potassium hydroxide effects solution in one-tenth the length of time with very little effect upon glass vessels. Nevertheless, with this modification the blank determination directed by the U. S. P. is still necessary.

Syrup Calcium Lactophosphates, N. F.—Occasionally ferments or develops growths. Increasing sugar content does not seem to prevent this. The use of 1 part of 40% formaldehyde solution in 10,000 parts of the syrup has proved effective in overcoming these defects.

Syrup Hydriodic Acid, U. S. P.—Caramelizes due to excessive acidity. Attempts to lower acidity by reducing proportion of hypophosphorous acid have resulted in appearance of free iodine in the syrup. The only practical method found so far is to decrease acidity through dilution with water allowed by a reduction of sugar content. Even so low a sugar content as 25% preserves well and a product with 35% sugar remains essentially colorless for a year. Possibly a buffer might be found which would reduce the acidity without decreasing the effectiveness of the hypophosphorous acid. Replacing the sugar with glycerin is satisfactory if the glycerin is free from butyric acid, otherwise a repugnant odor develops.

Syrup Iodo-tannin, N. F.—Assay process for iodine advisable as method of manufacture makes loss liable.

Syrup Wild Cherry, U. S. P.—Generally does not keep well unless sugar content is increased to insure gravity of not less than 1.34 at 25° C.

Tincture Aconite, U. S. P., and **Fluidextract Aconite, N. F.**—It is to be hoped that some established means of stabilizing these products will be introduced into the next revisions.

Zinc Acetate, U. S. P., and **Zinc Phenolsulphonate, N. F.**—Assay process is very tedious, should be replaced by more practical one, such as the ferrocyanide titration method.

Zinc Chloride, Oxide, Stearate and **Sulphate** and **Liquor Zinc Chloride, U. S. P.**—A more distinctive assay process is advisable, such as the ferrocyanide titration method.

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GRAVIMETRIC DETERMINATION OF LEAD IN SOLUTION OF LEAD SUBACETATE.*

BY JOSEPH L. MAYER.

The United States Pharmacopœia, on page 221, directs that Solution of Lead Subacetate be assayed for its lead content by the following procedure:

> "Place about 1 cc. of Solution of Subacetate, accurately weighed, in a 200-cc. volumetric flask, dilute with 50 cc. of recently boiled distilled water and add 50 cc. of tenth-normal oxalic acid. Agitate the mixture thoroughly for five minutes, fill to the mark with distilled water, shake and filter, rejecting the first 20 cc. of the filtrate. Add 5 cc. of sulphuric acid to 100 cc. of the filtrate, warm to about 70° C. and titrate the residual oxalic acid with tenth-normal potassium permanganate. Each cc. of tenth-normal oxalic acid corresponds to 0.01036 Gm. of Pb."

Due to the fact that the volumetric solutions employed in the assay must be frequently restandardized the method is time-consuming and I have therefore developed the following gravimetric one:

> Into a tared 50-cc. flask accurately weigh about 5 Gm. of the sample, then add 5 drops of C.P. HNO_3 and distilled water sufficient to make 50 cc. Add 10 cc. of this diluted solution to a 400-cc. beaker containing about 300 cc. of distilled water and heat nearly to boiling, after which add NH_4OH to incipient precipitation, then dilute HNO_3 (1:10) to redissolve the precipitate, avoiding more than a slight excess; to this nearly boiling solution, add 50 cc. of a 10 per cent potassium-chromate solution and stir thoroughly during the addition. The chromate solution should be nearly boiling and added to the lead solution by means of a pipette delivering 50 cc. in about 40 seconds. If the lead chromate is precipitated hot and stirred vigorously during the precipitation it will settle clear in 15 minutes or less, when it is ready to be filtered. Filter while hot, collecting the precipitate in a weighed Gooch crucible, and wash with boiling distilled water, until the wash water does not show the least

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* Read before the Kings County Pharmaceutical Society meeting, March 10th.