THE CHEMISTRY OF THE PHARMACOPOEIA.*

BY J. R. RIPPETOE.

Everyone must concede that the New Pharmacopoeia is a decided improvement over its predecessor, and everyone knows that the next one will be better still.

We are right in assuming that every point in the Pharmacopoeia is based upon facts or theories as they have been established. But in universal practice what one or a few have proven to their satisfaction does not always meet the requirements of the workshop. The ninth revision committee invited the coöperation of all interested and received much valuable assistance. This assistance will continue unofficially or indirectly at such meetings like this until the next revision is taken up. This leads me to suggest that there should be created continuous committees to carry on coöperative work, as is done by the Official Association of Agricultural Chemists. This association through appointed referees invites members and non-members to coöperate in trying out methods of analysis upon standard samples for the purpose of determining the practicability of the methods before making them official. It is not necessary for me to point out the advantages of such work.

Taking the substances of the Pharmacopoeia in alphabetical order, I beg to make the following comments:

Aspidosperma.—An alkaloidal standard should be established for this drug and its fluidextract. A good quality of drug should contain at least 1 percent chloroform soluble alkaloids when assayed by the method for Cinchona. Two samples assayed recently were found to contain 0.14 and 0.34 percent chloroform-soluble alkaloids, respectively.

Aconitum.—Our experience has been that methyl red indicator gives a better end-point but somewhat lower result than cochineal indicator.

Balsamum Peruvianum.—The assay for cinnamein directs that the residue be dried to constant weight at 100° C. This cannot be done since its boiling point is between 225 and 235° C. The ether should be allowed to evaporate at room temperature or gentle heat and the residue dried in a vacuum desiccator over sulphuric acid. Complete extraction of the cinnamein is preferred to decanting an aliquot of an ethereal solution especially in the hot summer months.

Cannabis.—The requirement, "yield of alcoholic extractive is not less than 8 percent," is too low. A good quality of drug will assay at least 12 percent.

Colocynthis.—The pulp is always found to contain more than 8 percent[1] ash, which would seem to be advisable as a requirement, that is, should yield not less than 8 nor more than 15 percent ash.

Colchicum Corm.—The assay method is very good for the seed but with the Corm incomplete removal of starch gives obstinate emulsions in the subsequent chloroform extraction. Using 10 Gm. of the drug instead of 15, retaining the volume of the liquids as now given and finally using 150 mils of the filtrate representing 5 Gm. of the drug, very good results are obtained.

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* Read before New York Branch, A. Ph. A., March 12, 1917.

[1] Rippetoe, *Amer. Jour. Pharm.*, May 1912, p. 197.

Extractum Taraxaci is directed to be made with 125 mils of alcohol and 875 mils of water while the fluidextract is made with diluted alcohol equivalent and glycerin. The reason for the different strength menstruums is not obvious.

Fluidextractum.—The abbreviation "Fldext." is awkward to write and not pleasing to the eye. "Flext." is much better.

Fluidextractum Cascarae Sagradae Aromaticum.—This preparation still remains one of the museum specimens. It is no doubt a fair estimate to say that for every 1000 gallons used not more than one is made according to the official formula. Glycerin has no value as a solvent and as a sweetening agent sugar is better and much cheaper. The flavor is not familiar to the public.

Fluidextractum Ipecacuanhae should yield "not less than 1.8 Gm. nor more than 2.2 Gm. of the ether-soluble alkaloids of ipecac." The drug from which it is directed to be made should yield "not less than 1.75 percent of the ether-soluble alkaloids of ipecac." To be consistent and permit of practical working the alkaloidal content of the fluidextract should be not less than 1.50 Gm. nor more than 1.75 Gm.

Hydrochloric acid is used in the menstruum and then in preparing the syrup from the fluidextract acetic acid is added. Is the additional acid necessary? If so the same acid should be used in both.

Fluidextractum Sennae.—Two varieties of drug are recognized but the Alexandria only is directed to be used in preparing the fluidextract, syrup and syrup of sarsaparilla compound, while both varieties are permitted to be used in the compound infusion and compound glycyrrhiza powder. Both varieties should be permitted for all purposes. Is there any method for determining whether one or the other variety has been used?

Methylis Salicylas.—A simple test, possibly not proper material for the Pharmacopoeia, but useful nevertheless for distinguishing the synthetic methyl salicylate from the oils of gaultheria and sweet birch is the froth resulting from agitation. Any froth produced by shaking immediately disappears on methyl salicylate, while on the oils of gaultheria and sweet birch it will remain for quite a few seconds.

Oleum Olivae.—A limit of free acid in this oil is very desirable.

Myrrh.—"Not less than 35 percent of myrrh is soluble in alcohol." This requirement is very indefinite as no method is given. As to extractive soluble in alcohol 25 percent is about the average yield in our experience.

Pulvis Glycyrrhizae Compositus should have an ash standard.

Resina Jalapae.—The methods for determining chloroform and ether-soluble matter are lacking in details. We are directed to "Add 1 Gm. of the powdered resin to 10 mils of chloroform (or ether) in a stoppered flask and shake the mixture occasionally during one hour. Then filter, evaporate the filtrate, etc." The operator is left in doubt as to washing, size of filter to use or any precautions to be observed.

Sapo.—The alcohol used for alkalinity determination should be directed to be previously neutralized. Separating the fatty acids for determining their iodine number by the method outlined is a very tedious process. Acidifying the aqueous solution, extracting with ether, washing the ether solution with water and evaporating at a low heat is much more expedient and practical. The acids may be

dried in a vacuum desiccator or over sulphuric acid and weighed before determining the iodine number.

Sapo Mollis.—Determination of the fatty acids and their iodine number are desirable for this preparation.

Sodii Phosphas Effervescens.—There should be a test for sugar and assay methods for the sodium phosphate and sodium bicarbonate. This comment applies to other official effervescent salts.

Spiritus Aetheris Nitrosi.—This preparation is directed to be preserved in "well-stoppered" bottles. Cork stoppered should be directed. Many druggists no doubt think that a glass stoppered bottle is "well stoppered" but the ethyl nitrite evaporates very rapidly, escaping from a glass stoppered bottle.[2]

Tinctura Cinchonae Compositae.—The use of red cinchona of high assay diluted to standard in the finished preparation will produce a preparation of varying strength with reference to the bitter orange peel and serpentaria.

Unguentum Hydrargyri Ammoniati.—An assay method for determining the ammoniated mercury content is desirable. Determining as the sulphide gives very good results.[3]

Unguentum Hydrargyri Oxidi Flavi.—Same remarks as above.

Zinci Acetas and Other Official Salts of Zinc.—The assay method is very faulty, due to the hot diluted nitric acid, on being added to the zinc sulphide, liberating sulphur which forms a gummy mass that holds some of the zinc and gives a low figure. Dissolving the sulphide in dilute hydrochloric acid and precipitating as the carbonate gives satisfactory results.

Zingiber.—Six varieties of ginger are recognized and fully described but only one, the Jamaica, is directed to be used in preparing the several preparations, excepting the oleoresin. Is there a chemical difference that eliminates the other five varieties, although they must meet the same requirements as to percentage of extractive?

I am indebted to Mr. Nathan Smith for valuable suggestions in preparing these comments.

LABORATORY SCHIEFFELIN & CO.,
NEW YORK.

[2] Rippetoe, *American Druggist*, Dec. 1911, p. 307.

[3] Rippetoe, *Am. Jour. Pharm.*, May 1910, p. 223.