

and he obtained for the treatment of his condition a preparation whose composition was known. For these, he paid \$2.50. In the other case, he would have obtained, for an unknown—to him—ailment, a box of tablets of unknown composition that might or might not have been of value. If the editor, in this instance, had had an incipient gastric cancer and decided to "treat it" in the cheapest way—by buying five cents worth of tablets—he would have saved \$2.45 and possibly lost—his life.

While, then, we cannot accept all of the arguments put forth by the *North American*, we believe that the editorial as a whole is an excellent one. It represents the attitude of the intelligent layman toward the "patent medicine" evil. That the medical profession is responsible for at least a part of the evil we must regretfully admit. The prescribing of unknown preparations has been a practice so common to the profession as to nullify to a large extent all efforts that are being made toward ridding the public of the nostrum evil. We cannot too often assert, however, that the medical profession does not believe that there is no place in commerce for simple home remedies. Neither can the medical profession object to any proprietary preparation solely on the ground that it is advertised in the lay press. What it does object to is the fraudulence that is apparently inseparable from the exploitation of such preparations when sold to the public.

NOTES ON CHEMICAL TESTS OF THE UNITED STATES PHARMACOPŒIA.

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(Concluded from page 76.)

RESORCINOL.—The description of its appearance should be changed to read "colorless or not more than slightly pinkish," as this substance acquires a color very readily on keeping. The melting point is an important criterion of purity and therefore should be given in the form of a requirement; the boiling point, on the other hand, is unnecessary for establishing purity or identity and would be impracticable for that purpose, for several reasons; moreover, the boiling point given is not sufficiently elastic for medicinal products. A concentrated solution (1 in 2) is seldom entirely colorless, as now required, but a 5 percent solution should appear colorless in a stratum of 1 cm. and should not be more than faintly acid to litmus paper. In the examination for an odor of phenol, care is required that a "gentle heat," defined by the U. S. P. to be 32° to 38° C., is not exceeded, otherwise an odor of phenol may be developed through partial decomposition.

SACCHARUM.—The characterization of sugar as "white" and its saturated water-solution as "colorless," applies only to small bulks. Sugar of commerce, to which no blue coloring matter has been added, and its concentrated solutions appear distinctly yellowish when viewed in large bulk. While account is taken by the U. S. P. of the possible presence of ultramarine and Prussian blue, the use of which for "facing" sugar is obsolete, a test is lacking for water-soluble

aniline colors, which are now more commonly used. In this respect it would probably be sufficient to require that only a yellowish, but no greenish or bluish color should be visible, when a cold-saturated water-solution is examined in a stratum of not less than 10 cm., also that in a stratum of 2 cm. the solution should appear colorless. As a test for glucose and invert-sugar ammoniacal silver nitrate is not generally regarded with favor, because of the risk of misleading results; most foreign pharmacopœias direct alkaline copper solution for their detection, e. g., the Swiss Ph. requires that 10 cc. of syrup (2:1), 1 cc. of caustic soda solution (sp. gr. 1.33 at 15°), and 1 cc. of a 10 percent water-solution of crystallized copper sulphate, if mixed at ordinary temperatures, should show within five minutes at most a greenish turbidity, but no separation of red cuprous oxide; the German Ph. requires that a mixture of 6 cc. of a water-solution of sugar (1+19) with 5 cc. of Fehling's solution, if heated until it boils up once, should not show a yellow or reddish deposit at once. In addition to the present tests of the U. S. P., tests for heavy metals, chlorides, and sulphates should be required. A limit of non-combustible impurities, probably 0.05 percent, should also be set.

SACCHARUM LACTIS.—The official test for adulteration with sucrose was taken from the German Pharmacopœia, fourth ed., but the fact that "diluted alcohol" of that authority is much stronger than that of the U. S. P. was overlooked, hence the occasional reports that cane sugar has been found in milk sugar, because of greater solubility of the latter in the weaker alcohol. With the following changes the test gives reliable results: 2 gm. of milk sugar, in fine powder, are shaken frequently at 15° C., during half an hour, with 20 cc. of diluted alcohol (containing 69 to 70 per cent, by volume, of absolute alcohol) and 10 cc. of the filtered liquid are evaporated on a water-bath to dryness; the residue, when dried at 100°, should not exceed 0.03 gm. Other substances soluble in weak alcohol will, of course, also be shown by this test. H. Leffmann proposes a simpler test for sucrose, as follows: 0.5 gm. of milk sugar and 1 cc. each of oil of sesame and concentrated hydrochloric acid are shaken together; if sucrose be present, the characteristic crimson coloration will be formed within half an hour.

SALICINUM.—A melting range of 198° to 201° could be required as a test of purity, a test for heavy metals might be added, and a limit of 0.05 percent of ash allowed.

SANTONINUM.—The melting range of santonin of good quality is well within the limits of 170° and 172°, which should probably be made a requirement. The test for readily carbonizable impurities is best made with 0.1 gm. of santonin and 2 cc. of sulphuric acid. Ash should not exceed 0.05 percent.

SAPO.—As large quantities of soap are used in dried form for official preparations, it would seem that this should be considered in the establishment of a standard for soap, particularly, as no method of drying is specified in cases where dried soap is directed. Soap liniment, for example, is likely to vary considerably in soap content, unless the allowable limit of water in the granulated soap is specified; it should certainly not exceed 5 percent in either powdered or granular soap. According to published reports, olive oil soaps, especially in powdered form, have sometimes been rejected because of failure to stand the official test for "absence of animal fats" (more properly "*soap* made from animal fats"). This test is faulty in failing to take account of a variation in water content of

soaps and in failing to specify to what temperature the alcohol-solution should be cooled, both of these factors influencing the result seriously. Trials with several specimens of olive oil soap, moist and dried, show that the test should be modified somewhat as follows: A solution in 25 cc. of alcohol, U. S. P. strength, of a quantity of soap equivalent to 0.65 gm. of water-free soap should not gelatinize if cooled to 20° C. The limit of impurities insoluble in alcohol, but soluble in water, may be reduced to about 1 percent, and the limit of substances insoluble in both alcohol and water to 0.2 percent. The official test for "limit of alkalinity" is unsatisfactory and should be replaced with a more stringent test for sodium hydroxide, which is not found in soap of the better grade. Such a test is conveniently combined with the preceding one, by dissolving about 10 gm. of soap in 100 cc. of alcohol, washing insoluble matter with hot alcohol, etc.; the filtrate should not be reddened by phenolphthalein.

SAPU MOLLIS.—The official limit test for "free alkali" is inconclusive because it fails to distinguish between KOH and K_2CO_3 . The latter is comparatively unobjectionable in moderate quantity and is taken care of in the succeeding test for limits of alcohol-insoluble matter, but some uses of soft soap in dermatology apparently require presence of a slight amount of uncombined KOH, which should, however, be limited to about 0.25 percent. It is no great hardship to make a soap containing not less than 0.1 and not more than 0.25 percent of KOH, as determined by titration of a filtered alcohol-solution with N/10 acid, with phenolphthalein as indicator. Uniformity of composition could be further promoted by requiring either a minimum percentage of fat acids or by limiting the loss in weight as determined by the official method given under *Sapo*; the loss should not exceed 50 percent.

SODII ACETAS.—Doubtless because of an erroneous impression that solutions of the pure salt in water are not reddened by phenolphthalein, the requirement is made that a water-solution of the salt "should not affect phenolphthalein." The fact that chemically pure sodium acetate is alkaline to phenolphthalein in water-solution was pointed out by the writer to the revision committee before the eighth revision, but was either overlooked or disbelieved. Those who still doubt this can easily prove this for themselves by crystallizing the salt from a water-solution containing a slight excess of acetic acid and thoroughly washing the crystals with neutral distilled water. It will be found that this purified salt, when dissolved in water, will give a color with phenolphthalein. For comments on the assay see under *Potasii Acetas*.

SODII ARSENAS.—The most satisfactory method of assay is probably that of Williamson, as given in Sutton's *Volumetric Analysis*, 10th ed. (1911), consisting in the reaction of arsenic and hydriodic acids in a strongly acid mixture, resulting in the formation of arsenous acid and free iodine, the latter being titrated with thiosulphate. The method has been used with satisfactory results in this laboratory.

SODII BENZOAS.—Before weighing for an assay, the salt should be dried to a constant weight at about 120° C., which may require several hours, and a carefully made product should not lose more than 5 percent in weight by this treatment. The assay method is unpractical, because the charred mass, being in hard and compact pieces, is not extracted thoroughly by boiling water or even by boil-

ing weak acids, unless it is first reduced to a fine powder. A more satisfactory method is that of direct determination of the benzoic acid, by shaking it out with chloroform from an acid mixture and weighing it after evaporation of the solvent. To insure complete extraction it is necessary that the amount of water in the mixture be very small in comparison to the bulk of chloroform, that the shaking be vigorous and prolonged, and that not less than three successive portions of chloroform be used. Evaporation of the chloroform should be without the aid of heat and the residual benzoic acid should be dried in a desiccator before weighing.

SODII BICARBONAS.—While the salt of commerce will readily test 99 percent by the official method of titration, the amount actually present is usually somewhat less. With more exact methods of determination replacing the present one, a minimum requirement of 98 percent would be feasible. The requirement that the salt must produce a “perfectly clear” solution in water is impracticable and conflicts with the general provisions in “Introductory Notices” of the U. S. P., under “Solubility Tests,” wherein traces of insoluble impurities are permitted. Results of the test for normal carbonate vary with the manner in which the details are carried out. If the solution is cooled much below 15°, stringency of the test will be decreased and the manner of adding the acid may cause considerable variation in the amount of carbon dioxide given off. In the interest of uniformity it is recommended that the temperature of the solution be adjusted to 15°, then poured, all at once, upon the 0.2 cc. of normal hydrochloric acid and the phenolphthalein, contained in a test tube of 18 to 20 mm. diameter. A titration of sodium bicarbonate with methyl orange as indicator, as officially directed, of course includes also the normal carbonate present. For determination of both, the following method of G. Lunge includes several features often ignored, but necessary for accurate work: About 5 gm. of the salt are dissolved in not more than 100 cc. of distilled water (boiled and cooled), at a temperature not exceeding 20° C., without agitation other than gentle stirring with a glass rod. About 10 gm. of pure sodium chloride are then dissolved in this liquid, which is then cooled to almost 0° C., phenolphthalein is added and normal hydrochloric acid, with the tip of the burette below the surface of the liquid, until the color is just discharged. Each cc. (O=16) corresponds to 0.1061 gm. of Na₂CO₃. An aliquot portion of this titrated solution is then titrated with methyl orange as indicator, in the usual manner, and the number of cc. of normal acid used in the first titration subtracted from the number required in the second. The remaining number of cc. represent the NaHCO₃ in the sample, each cc (O=16) corresponding to 0.08401 gm. Another fairly accurate and expeditious method consists in heating a known weight of the salt, dried over sulphuric acid before weighing, at a temperature somewhat below red heat, until the weight is constant and calculating the NaHCO₃ from the loss of water and carbon dioxide.

SODII BORAS.—Comments under *Sodii Bicarbonas* regarding “perfectly clear” solutions apply also to this salt. For an assay, the well known method of titrating a water-solution of the salt with hydrochloric acid, with methyl orange as indicator, is satisfactory, each cc. of normal acid (O=16) corresponding to 0.101 gm. of Na₂B₄O₇. It is not advisable to calculate the results as Na₂B₄O₇.10H₂O, as the salt, particularly when powdered, is often more or less effloresced, but the

sum of the percentages of $\text{Na}_2\text{B}_4\text{O}_7$, and of H_2O (determined by loss of weight at red heat) should not be less than 99 and the percentage of H_2O should not be more than 49 percent in crystals and not less than 42 percent in the powdered salt.

SODII BROMIDUM.—The standard might be raised to a minimum of 98.5 percent. The salt should be powdered and dried at 100° to 110° to a constant weight before weighing it for the titration with silver and the allowable water-content should be limited to 4 or 5 percent. No limit of moisture is now specified in the U. S. P., but this is desirable because it is possible to make a crystallized salt containing theoretically 2 molecules, or 25.9 percent, of water. Comments under *Potassii Bromidum* apply also to this salt.

SODII CHLORIDUM.—Results of assays by the official methods are seriously affected by presence of calcium and magnesium chlorides, which are among the common impurities in ordinary salt; the more of these is present, the higher will be the apparent NaCl content. Unless they are present only in traces, quantitative determination of them is required, as also of sulphate, another common impurity, in order to ascertain the actual percentage of sodium chloride in this salt.

SODII CITRAS.—There is no good reason for an official allowance of 3 percent of impurities other than water in this salt; a standard of 99 percent is not too high. A test for tartaric acid should be added. Comments under *Potassii Acetas* concerning the assay method apply also to this salt. Because of variability in crystal-water contents, the percentage of *anhydrous* salt found by the assay should be added to the percentage of water, determined by drying at 150° C. The sum should not be less than 99 and the percentage of water should not be more than 3 percent above the theoretical amount in crystals nor more than 5 percent below the theoretical amount in the granular or powdered salt.

SODII HYPHOSPHIS.—The requirement that the salt should not be alkaline to phenolphthalein conflicts with the limit test for alkalis and should be omitted. For comments on assay methods see under *Potassii Hypophosphis*.

SODII IODIDUM.—It should be allowed to contain not more than 5 percent of crystal-water, which is determined by drying at 100° to 110° C. Comments under *Potassii Iodidum* are applicable also to this salt.

SODII NITRIS.—The standard could be raised to 95 percent.

SODII PHENOLSULPHONAS.—For an assay the following method of Smith and Frey, based on the determination of phenol-p-sulphonic acid, may be used. From 0.24 to 0.25 gm. of the salt is dissolved in 50 cc. of water in a glass-stoppered flask (250 cc. volumetric flask answers best), 50 cc. of N/10 bromine solution are added, then 5 cc. of hydrochloric acid, and the stopper quickly inserted. The mixture is then allowed to stand, with occasional shaking, at a temperature of 20° to 25° C. for not less than 10 nor more than 15 minutes. The stopper is then raised just enough to introduce, without loss of bromine vapors, a solution of 2 gm. of potassium iodide in 5 cc. of water. The mixture is thoroughly shaken in the stoppered flask and the liberated iodine titrated with N/10 thiosulphate solution. The number of cc. required are subtracted from the number of cc. of N/10 bromine solution taken. Each cc. of the remainder corresponds to 0.005804 gm. of $\text{NaC}_6\text{H}_5\text{O}_4\text{S}\cdot 2\text{H}_2\text{O}$ (O=16). If the liquid remains clear or nearly so throughout the determination, the sample may be considered sufficiently

free from interfering impurities for the results to be dependable. The salt of the market sometimes contains phenol and possibly other compounds that form insoluble bromine derivatives under the conditions of the determination and the presence of these affects the accuracy of the method in proportion to their quantity, but a carefully purified product should be practically free from them. This question may be settled by a preliminary test as follows: Addition of bromine water to 5 cc. of a cold water-solution of the salt (1 in 100), until the liquid is permanently yellow, should remain clear for two minutes after the last addition.

SODII PHOSPHAS.—Besides the impurities for which official tests are given, this salt usually contains considerable quantities of sodium sulphate. Chlorides are usually present only in traces. The various impurities must be considered in a choice of methods of assay, because of the possibility of their affecting the accuracy of results. In calculating the percentage of sodium phosphate from a determination of phosphoric acid, the plan proposed under *Sodii Boras* should be followed whenever the salt tested does not contain the full amount of crystal-water and as particularly the granular salt loses water very readily, the U. S. P. should provide for a limited shortage of crystal-water.

SODII PHOSPHAS EXISCCATUS.—It should be allowed to contain not more than 4 or 5 percent of absorbed water.

SODII PYROPHOSPHAS.—The test with molybdate solution for distinction from orthophosphate is misleading, since orthophosphate is formed from pyrophosphate through contact with the nitric acid in the reagent. Difference in the color of precipitates with silver nitrate is more reliable for differentiation and also a sufficiently delicate test to exclude excessive amounts of orthophosphate.

SODII SALICYLAS.—A substance that is permitted to have a "faint pink tinge" can scarcely be expected to produce entirely colorless solutions in all concentrations; however, a freshly-made 5 percent solution of the salt should appear colorless in a stratum of 2 cm. The purest products of the market are distinctly alkaline to litmus, though not to phenolphthalein, and the requirement that the salt "should slightly redden blue litmus paper" excludes all specimens that contain less than about 1 percent of sodium acid salicylate, $\text{NaC}_7\text{H}_5\text{O}_9 \cdot \text{C}_7\text{H}_6\text{O}_4$. If for some purposes a salt having an acid reaction is preferable, it is certain that for others the purer normal salt, which has a slightly alkaline reaction, is to be preferred. It would, therefore, seem advisable that the Pharmacopoeia allow also a neutral and a slightly alkaline reaction. A test based on the decolorization of iodine is preferable to the official test for sulphites, as sodium salicylate often contains unobjectionable traces of sulphates, the presence of which makes the test inapplicable in its present form. Comments on methods for the assay of Sodium Benzoate apply also to this salt.

SODII SULPHAS.—To determine the percentage of actual sodium sulphate, it is usually most convenient to determine the sodium chloride, which is likely to be the chief impurity, and the water, then calculate the remainder as anhydrous sodium sulphate.

SPARTEINAE SULPHAS.—The reasons for the widely varying figures given by different authorities as the melting point of this salt require investigation. These vary from 136° to 152° . Variations from 132° to 150° have been noted in this

laboratory, all specimens meanwhile conforming in other respects to the U. S. P. standard. The odor of free sparteine is considered by some persons to resemble that of aniline and as for that reason the latter might be used as an adulterant or substitute, a test for it is directed by several pharmacopœias, somewhat as follows: A mixture of about 0.1 gm. of sparteine sulphate, 0.5 cc. of chloroform, and 0.5 cc. of alcoholic potash solution (about half-normal strength) should develop no isonitrile odor when heated.

SPIRITUS AETHERIS NITROSI.—The U. S. P. gives a standard of strength only for the freshly made spirit and it would seem that it might still be considered to conform to the U. S. P. standard after having lost the greater part of its ethyl nitrite on keeping. The British and Netherlands Pharmacopœias allow a deterioration from the original strength of not more than 30 and 20 percent, respectively. A similar provision should be made by the U. S. P., with the requirement that the spirit should not be dispensed if it contains less than a stated amount of ethyl nitrite, perhaps 3.5 percent.

SPIRITUS AMMONIAE.—Instead of merely stating the specific gravity to be "about 0.808 at 25° C.," it would be better to definitely require it to be not more than 0.805, as a higher specific gravity indicates presence of an excessive amount of water. The permanganate test, as given under Ammonia Water, requires slight changes to make it applicable to the spirit, as the alcohol in the mixture decolorizes permanganates; the liquid, which is warm from the reaction of ammonia and sulphuric acid, should be cooled to about 20° C. before addition of the permanganate and this should be increased to 0.2 cc. For the titration the spirit is preferably weighed in a flask containing water, to minimize the loss of ammonia through volatilization.

SPIRITUS GLYCERYLIS NITRATIS.—Upper as well as lower limits of nitroglycerin contents should be specified for such a potent substance, since an exact 1 percent is unattainable. It might be advisable to permit a variation of 1 to 1.05 percent, or 0.97 to 1.02 percent. The second reference in the U. S. P. to the specific gravity contradicts the first and should be omitted. For an assay the method of the Danish Pharmacopœia seems well adapted; it is as follows: To about 10 gm. of the spirit add in a flask of suitable size 2 cc. of caustic soda solution (1 in 10). After a few hours warm the liquid and finally evaporate the alcohol on a water-bath. Dissolve the residue in 10 cc. of water, add 2 cc. of hydrogen peroxide solution (3%) and warm the liquid at first gently, then heat it to boiling. Transfer it to a 500 cc. boiling flask, using 10 to 15 cc. of water for rinsing the first flask. Add 12 cc. of a mixture of 1 volume of sulphuric acid and 2 volumes of water, then 5 gm. of reduced iron. Insert in the neck of the flask a test-tube filled with cold water and warm the flask at such a rate that the liquid will boil in 4 minutes, as shown by the dripping of water from the test-tube. Boil the mixture about 1 minute, then add 150 cc. of water and 25 cc. of caustic soda solution (1 in 2). Connect the flask quickly with a condenser and distill the ammonia into a receiver containing 25 cc. of N/10 hydrochloric acid. Titrate the excess of acid and calculate the percentage of nitroglycerin from the amount of ammonia found.

STRONTII BROMIDUM.—It is not "very deliquescent" unless it contains abnormally large quantities of calcium halides, nor is it "occasionally efflorescent,"

either when pure or when it contains the usual impurities within U. S. P. limits. The effloresced appearance of some crystalline products of the market is generally caused by drying at elevated temperatures. A salt of U. S. P. standard of purity, which may contain small amounts of calcium compounds, is slightly deliquescent if it does, but is permanent in the air when free from them. Titration of the hydrated salt with silver nitrate is not always sufficient to determine the percentage of $\text{Sr Br}_2 \cdot 6\text{H}_2\text{O}$ in it. Only when the salt is practically free from all impurities except strontium chloride and contains just the theoretical amount of water will the official method give fairly accurate results. It would be quite feasible, however, for the U. S. P. to demand almost total absence of calcium and then only the variation in water content need be considered. To overcome this it is only necessary to dry the salt to a constant weight at 180° and titrate a weighed quantity of the anhydrous salt. The ratio of strontium bromide and chloride can then be readily calculated from the amount of silver nitrate solution required for precipitation.

STRONTII IODIDUM.—Because of variability of water contents and possible presence of calcium salts, titration with silver nitrate is not a very suitable assay method. One of the several well-known methods for the direct determination of iodine in presence of chlorine would be preferable, combined with a determination of strontium if much calcium is present.

STRONTII SALICYLAS.—Concerning the requirement that “its aqueous solution should be colorless,” comments under *Sodii Salicylas* apply also to this salt. An assay based on the weight of sulphate formed is not reliable, as it includes such impurities as calcium salts and strontium or alkali chlorides, which may be present and for which no tests are given. A more useful quantitative determination would be that of the salicylic acid, by a method such as is discussed in these notes under *Sodii Benzoas*.

STROPHANTHINUM.—Strophanthin-Kombé of commerce is amorphous, not crystallized as this substance is described in the U. S. P. The melting point should be omitted, as official strophanthin is a mixture of variable composition.

STRYCHNIA.—The melting points of strychnine and its official salts are variable because of partial decomposition by the required heat; determination of them is needless for identification and valueless for ascertaining purity. As traces of harmless impurities other than brucine, sometimes present in strychnine and its official salts, may produce an orange color with concentrated nitric acid, it is preferable to modify the test for brucine as has been done by some other pharmacopœias, somewhat as follows: 1 cc. of a mixture of equal volumes of nitric acid and water, mixed with about 0.1 gm. of strychnine or its official salts, may produce a yellow, but no red or reddish color. The delicacy of the test is not appreciably diminished by the change.

SULPHONETHYLMETHANUM.—The melting point should be replaced by a range of 75° to 77° , which limits should be definitely required as a test of purity. In the permanganate test 20 cc. of the filtrate from the preceding test should be taken and 0.05 cc. of N/10 potassium permanganate (measured with a 1 cc. pipette). As the test now stands, it is too vague to be of use.

SULPHONMETHANUM.—It should be required to melt between 125° and 127° and the permanganate test should be made as described in the preceding.

SULPHUR LOTUM.—This, and sublimed sulphur, from which it is made, are mixtures of varieties soluble and insoluble in carbon disulphide and the statement "readily soluble" should be changed to "partially soluble." Determination of the percentage of actual sulphur, by oxidation to sulphuric acid and weighing as barium sulphate, is not generally required to ascertain if a given specimen conforms to the minimum standard of 99.5 per cent. An indirect determination, by deduction of the amount of non-volatile matter found, is generally sufficient and likely to be more accurate with the pharmaceutical grades of sulphur.

SULPHUR PRAECIPITATUM.—The requirement as to non-volatile matter is too stringent. Other pharmacopœias are more lenient; the German, e. g., allows 0.5 percent. See also under *Sulphur Lotum*.

SULPHUR SUBLIMATUM.—See comments under *Sulphur Lotum*.

SYRUPS ACIDI HYDRIODICI.—In the assay, the syrup should be diluted with considerably more water than is directed, before admixture with silver nitrate, to prevent reaction of the latter with the hypophosphorous acid present. Insertion of a test for excessive amounts of other halogens would be desirable.

SYRUPUS FERRI IODIDI.—The comments under the preceding apply also to this preparation.

TEREBENUM.—It appears to be still an open question what the composition should be of the mixture of hydrocarbons known as terebene. This is illustrated by the boiling ranges given by different authorities: 160° to 170° (U. S. P.); 156° to 180°, not over 15 percent below 165° (Brit. Pharmacopœia; Brit. Phar. Codex); 156° to 160° (Hager's Phar. Praxis); 155° to 160° (Schmidt's Phar. Chemie); 170° to 185° (Power and Kleber, in 1894). Dipentene, which is generally considered the chief constituent, boils at 175° to 176° (Schmidt), or at 181° to 182° (Wallach; Brass), and it is therefore not likely that the U. S. P. product contains very much of it. If dipentene is the most important constituent, therapeutically, which appears not to have been demonstrated so far, then the boiling range proposed by Power and Kleber should certainly be specified in preference to that of the U. S. P. The subject requires further investigation, both pharmacological and chemical. A change in the boiling interval would require also a change in specific gravity limits. The official directions for determining resinous substances do not lead to reliable results, as exposure to air during evaporation causes formation of resins and greatly increases the amount of non-volatile residue. By vacuum evaporation at about 100° residues of 0.2 to 0.3 percent were usually obtained from samples that yielded 5 to 10 times as much when the U. S. P. directions were followed. In absence of a suitable vacuum apparatus atmospheric oxidation can be prevented to a large extent by transferring the residue remaining in the flask used for the boiling point determination to an evaporating dish, with the help of ether, evaporating rapidly or a water-bath, then drying at 100°. From 0.5 to 0.7 percent of resin were obtained in this manner.

TERPINI HYDRAS.—The official statement that it is permanent in the air does not agree with practical experience, which shows that it is somewhat efflorescent and often does not contain fully 1 molecule of crystal-water. For that reason a determination of the melting point, as a test for organic impurities, is preferably made after removal of the water by drying the finely powdered substance over

sulphuric acid to a constant weight, as the melting point of the hydrate varies with the degree of hydration. Anhydrous terpin should melt between 102° and 105°.

THYMOL.—The specific gravity should be stated as being "about 1.030." In place of the requirement of an impossibility, that a crystal leave *no* residue on volatilization, it would be better to require that a quantity of not less than 1 gm. should leave not more than 0.5 mg. of residue. An alcohol-solution (1 in 20) should be required to be neutral to litmus paper wetted with water.

THYMOLIS IODIDUM.—Although chemically pure dithymol diiodide would contain 46.2 percent of iodine, the products of few manufacturers meet the U. S. P. specification requiring a content of 45 percent, owing to the costly methods of manufacture necessary to attain that standard. Admixture with chlorine derivatives of thymol usually brings the iodine contents down to from 42 to 43 percent. A minimum standard of 42 percent would, therefore, seem to be required in the dried product. An allowance of not more than 1 percent of moisture should also be made, as this substance may appear dry and yet contain a large amount of moisture. G. M. Beringer has pointed out that thymol iodide of the market is a mixture of several organic iodine compounds differing in solubility. This fact need cause no surprise, as it has been known for many years (Patent of Farbenfabriken verm. Bayer & Co., 1889) that thymol iodide is converted into a white iodothymol (in which iodine is considered to be linked directly to carbon) through several agencies, such as treatment with caustic alkalies, thiosulphates, etc. It seems probable that appreciable quantities of iodothymol are formed by the usual procedures of preparing thymol iodide and it is not unlikely that further conversion is induced by the action of light and heat during washing, drying, and afterwards, as temperature and light are known to influence the color of the product to a marked degree. The drug trade demands chiefly a product of light buff color and it may be found on investigation that this contains a much larger proportion of iodothymol than the dark, reddish-brown product. Thymol iodide should not yield more than 0.5 percent of ash; the present allowance of 3 percent is entirely too liberal. Differences in methods for the determination of the iodine have given rise to controversies concerning iodine contents. The writer is indebted to Mr. Henrik Knudsen for calling his attention to Groeger's method for the determination of iodine in presence of chlorine, the following adaptation of which has been found in this laboratory to be reliable: Mix thoroughly in a mortar 0.2 to 0.25 gm. of dried thymol iodide with about 3 gm. of dried sodium carbonate and transfer the mixture to a crucible. Remove traces of the mixture adhering to the mortar with about 1 gm. more of the sodium carbonate and cover with it the contents of the crucible. Heat the mixture moderately, gradually increasing to, but not exceeding, dull redness, in the covered crucible, until the mass is completely carbonized. When sufficiently cooled, extract the residue with boiling water and wash it on a filter with boiling water until the washings cease to react with silver nitrate. Heat the combined liquids, which should measure about 150 cc., on a bath of boiling water and add a solution of potassium permanganate (1 in 20) in small portions, until the hot liquid is permanently pink. Add just enough alcohol to remove the pink tint, cool the liquid to room temperature, and dilute it to 200 cc. Mix

well and filter through a dry filter, 9 to 10 cm. in diameter, and reject the first 50 cc. of filtrate (to avoid any error through adsorption). To 100 cc. of the subsequent clear filtrate add about 1 gm. of potassium iodide and an excess of diluted sulphuric acid, then titrate the liberated iodine with N/10 sodium thiosulphate. Each cc. (O=16) corresponds to 0.002115 gm. of iodine.

VANILLIN.—The results of G. A. Menge, who found 5 commercial samples to have an average melting interval of 81.9° to 82.5° (corr.), with only slight variations, indicate that the figures of the U. S. P., 80° to 81°, which are also given by most other authorities, are too low and should probably be replaced with a required interval of 81° to 83°. Adulteration with such substances as acetanilid, terpin hydrate, coumarin, etc., which is occasionally reported, is detected most conveniently by deviations in the melting point.

VERATRINA.—The melting point should either be omitted or given as a roughly approximate figure, since it must necessarily vary considerably with a mixture such as this. Presence of many foreign alkaloids may be detected, according to various authorities, by addition of platinic chloride to an alcohol-solution of veratrine (1 in 20); no precipitate or turbidity should be produced.

ZINCI ACETAS.—Stringent official tests for chlorides and sulphates require the salt to be practically chemically pure in order to meet the U. S. P. requirements, which raises its cost unnecessarily. If the dilution of the solution for these tests be extended to 1 in 200, the requirement can be met more readily. A salt of this degree of purity, unless it is found to contain alkali or alkali earth compounds, for which no tests are given, scarcely requires quantitative determinations to prove conformity to the specified minimum standard. Precipitation as sulphide and weighing as such is doubtless the most accurate of the usual methods.

ZINCI CARBONAS PRAECIPITATUS.—To prepare solutions for making tests of purity hydrochloric acid is to be preferred to sulphuric acid and enough should be taken to dissolve the salt completely. When the official directions are followed, some impurities may be left on the filter and escape detection; e. g., lead, if present, will be filtered out almost entirely, as sulphate. The weight obtained as a result of the official assay includes, besides the allowed traces of sodium carbonate, iron compounds, and other heavy metals, also other fixed impurities of which no account is taken in the tests of purity, such as basic zinc sulphate, presence of which cannot be entirely avoided, and sodium sulphate, which may be present through incomplete washing of the salt. To determine the zinc combined as basic carbonate, the official method for the assay of Zinc Oxide would be more suitable, with deduction of the acid required to neutralize any sodium carbonate in the sample, but the minimum standard would have to be lowered to something like 70 percent of Zn O. Possible presence of alkali earth carbonates would also have to be considered in the use of this method of determination.

ZINCI CHLORIDUM.—It is not feasible to determine the water contents of this salt by ordinary methods, as the heat required to render it anhydrous also expels appreciable quantities of hydrochloric acid and probably also volatilizes some zinc chloride. It is, therefore, impracticable to base the standard of purity on the anhydrous salt, as is done in the U. S. P. It would be better to base it upon the salt in its original condition, but in view of its strongly hygroscopic nature the minimum requirement should probably not be placed higher than 90 percent of

Zn Cl₂. Suitable tests to exclude excessive amounts of alkalis and alkaline earths should then be added. The melting point varies much in accordance with variation in water contents, which makes the official melting point inapplicable. A water-solution of the salt (1 in 20) cannot be expected to be "clear or at most only very slightly opalescent," as the temperature required to remove most of the water causes formation of enough basic salt to produce a rather turbid solution. The test for sulphate is so stringent as to increase the cost of the salt unnecessarily.

ZINCI OXIDUM.—The official test for chlorides is rather too stringent; traces are unobjectionable and should be allowed.

ZINCI PHENOLSULPHONAS.—In view of the impurities this salt may contain, precipitation as sulphide is probably the most reliable of the ordinary methods for a zinc determination. The medicinal value should doubtless be based chiefly on the zinc content and only secondarily on the phenolsulphonic acid content. The latter may be determined by the method recommended under *Sodii Phenolsulphonas*, the quantity of sample being increased in proportion to the greater molecular weight.

ZINCI STEARAS.—A residue not exceeding 0.5 percent should be allowed in the test for alkalis and alkaline earths, the present requirements being impracticable. The present limits specified for zinc contents are also impracticable and should be replaced by a range of 13 to 15 percent of ZnO. In presence of alkalis and alkaline earths the official assay method gives too high results and the sulphide method, after elimination of the fat acid, would be preferable. To the tests for impurities one should be added to limit contamination with lead and other heavy metals. The stearic acid, separated from the salt by heating with weak hydrochloric acid and thoroughly washed with hot water, then kept in contact with ice for 2 hours or at 10° C. for 24 hours, should meet the melting point requirements of the U. S. P. for stearic acid.

ZINCI SULPHAS.—The small amount of zinc chloride, which the U. S. P. allows to be present in this salt, may impart an acid reaction to alcohol, being soluble in it. Hence the official test for free acids is not reliable. A better and also simpler test consists in slightly coloring a water-solution of the salt (1 in 20) with methyl orange. No acidity should thus be shown.

ZINCI VALERAS.—Loss of valeric acid during unavoidable exposure to the air renders the salt partially insoluble in water and it may then no longer be acid to litmus, as officially specified. On account of the instability of this salt, the requirement of a minimum of 99 percent of normal salt can be met only by freshly made products, unless they are kept in air-tight containers. It would be unfair to apply the rigid pharmacopoeial specifications to specimens that have been on the pharmacist's shelves for some time.

The author deems it advisable to state more clearly than was done at the beginning of this series of notes, that he alone is responsible for the views and opinions expressed in the several installments thereof. While these views and opinions were formed largely as a result of the facilities extended by the laboratories of the Powers-Weightman-Rosengarten Company, of Philadelphia, Pa., they do not necessarily coincide with those of the officers of said company.