

Contributed and Selected

NOTES ON CHEMICAL TESTS OF THE UNITED STATES PHARMACOPOEIA.

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(Continued from page 1273.)

HYDRASTINA.—The melting point of the U. S. P. is the same as given by some authorities for the chemically pure alkaloid and medicinal specimens must be expected to vary somewhat from this figure, especially since allowance of appreciable quantities of impurities is implied by the description "white to creamy-white." The intention of the test for distinction from hydrastinine is not stated clearly enough; a solution of 0.1 gm. of hydrastine in 10 cc. of diluted sulphuric acid develops a blue fluorescence on addition of a few drops of N/10 potassium permanganate, but no fluorescence should be visible before addition of the reagent. Some authorities give a test for berberine; an aqueous solution of hydrastine (1 in 20), made with aid of a slight excess of hydrochloric acid, should not be reddened by addition of chlorine water.

HYOSCINAE HYDROBROMIDUM.—While the U. S. P. does not explicitly specify the laevorotatory modification, the melting point given practically excludes the optically inactive form. Since, however, determinations of melting points as high as 190° are notoriously untrustworthy, it may be advisable for the U. S. P. to require definite limits of optical rotation, to exclude excessive quantities of the optically inactive *i*-scopolamine. The German Pharmacopoeia directs a test for apatropine, as follows: A mixture of 5 cc. of a 1 percent. water-solution of the salt and a drop of a water-solution of potassium permanganate (1 in 1000) should not be completely decolorized within 5 minutes. The sulphuric acid test for "carbonizable impurities" should be made with about 0.1 gm. of the salt and 1 cc. of the acid. In the test for morphine, a rather superfluous test, "any color" should be changed to "a dark red color," as an orange color is produced with the pure salt, due to liberation of bromine.

IODIFORMUM.—A test for alkalis, as well as for acids, should be made with litmus paper. Adulteration with sulphur, sometimes reported, may be detected by dissolving the sample in alcohol, in which sulphur is nearly insoluble.

IODUM.—The specific gravity is, of course, to be regarded only as a statement of one of the physical characteristics of chemically pure iodine and not as a rigid requirement, but this, as in many similar cases, should be indicated by the diction or by a general explanation in an appropriate place. Instead of the statement, "leaving no residue" a requirement of a limit of 0.1 percent. of non-volatile matter should be made. The statement under "Assay," that titration with thiosul-

phate, with the prescribed calculation of results, gives the percentage of pure iodine, is not strictly accurate, as it ignores the ever-present iodine chloride; specimens containing this impurity within allowed limits sometimes test as high as 100.5 percent. by the official method.

LIQUOR ACIDI ARSENI.—To allow for unavoidable slight inaccuracies in the weighing of ingredients, loss in handling, deterioration on keeping, etc., a slight variation in strength should be officially recognized. The "rubric" calls for an *inflexible* 1 percent. and the assay for a *minimum* of 1 percent. of As_2O_3 . The former is, strictly speaking, a requirement of an impossibility, while the latter is an unsafe one, as it provides no *upper* limit. A requirement that the solution contain not less than 0.98 and not more than 1.01 percent of As_2O_3 would probably be acceptable to everybody concerned.

LIQUOR ARSENI ET HYDRARGYRI IODIDI.—The remarks under the preceding apply also to the arsenic and mercury contents of this preparation and official methods for their quantitative determination should be provided; additional determination of the iodine is also desirable.

LIQUOR FERRI SUBSULPHATIS.—A more reliable means for distinguishing this from the official solution of normal ferric sulphate should replace the time-honored test with sulphuric acid, which has been found misleading. The following simple test has been found more satisfactory: A mixture of 1 cc. of the solution and 40 cc. of water is heated until it begins to boil; a turbid mixture is obtained with the subsulphate, a clear solution with the tersulphate solution.

LIQUOR FORMALDEHYDI.—This solution, as found in commerce, contains a variable quantity, up to 14 percent., of methyl alcohol, the presence of which is not only unobjectionable but desirable, as it retards or prevents formation of para-formaldehyde. For this reason the specific gravity of solutions of official strength is often considerably lower than the U. S. P. limits, sometimes as low as 1.064 at 25°. The products obtainable in this market almost always contain traces of calcium sulphate, which is not allowed by the U. S. P., but to which no valid objection can be made.

LIQUOR HYDRARGYRI NITRATIS.—The percentage of mercury is determined most conveniently by titration with N/10 sulphocyanate, with ferric alum as indicator.

LIQUOR PLUMBI SUBACETATIS.—When adjusted to the required lead content by the official assay method, the specific gravity of the solution has been found to vary from 1.235 to 1.250 at 25°.

LIQUOR POTASSII ARSENI.—The comments under *Liquor Acidi Arsenosi* regarding the arsenic content apply here also.

LITHII BENZOAS.—In testing this and other official lithium salts for other alkalis, amyl alcohol boiling between 128° and 132° has been found as serviceable as the specified article boiling at 132°, which is not readily obtainable. For the quantitative conversion of this and other official lithium salts, sulphuric and nitric acids, as directed in the U. S. P. under *Lithium Citrate*, have been found preferable to ammonium sulphate. It is advisable also to use platinum instead of porcelain crucibles for such tests, because of the reaction of lithium carbonate with silicates at high temperature.

LITHII BROMIDUM.—The salt is not always alkaline, as stated, but is neutral when free from an excess of alkali or acid. For titration with silver nitrate it should be dried to a constant weight at 150° and no attempt should be made to weigh exactly 1 gm. of the dried salt, as it is too hygroscopic to be weighed otherwise than in a stoppered bottle. For additional comments see under *Lithii Benzoas*.

LITHII CITRAS.—A 5 percent. solution of a salt free from acid citrate is more than “faintly” alkaline to litmus. A temperature of 180° is preferable to 150° for making the salt anhydrous previous to the quantitative conversion into sulphate; at the lower temperature a constant weight cannot be reached in a reasonable length of time. For additional comments see under *Lithii Benzoas*.

LITHII SALICYLAS.—While this salt is officially required to be neutral or slightly alkaline to litmus, it is more than slightly alkaline to this indicator when free from acid salicylate. The salt of the market contains crystal-water corresponding approximately to the formula $\text{LiC}_7\text{H}_5\text{O}_3, \frac{1}{2}\text{H}_2\text{O}$, of which the Pharmacopoeia takes no account. It becomes anhydrous at 100° and should, therefore, be dried to a constant weight at that temperature before it is weighed for the quantitative determination as sulphate. For additional comments use under *Lithii Benzoas*.

MAGNESII CARBONAS.—The test for calcium should be made with enough ammonium oxalate to prevent precipitation of magnesium oxalate, in this case with about 5 cc. of the official test solution. Anhydrous magnesium oxide being very hygroscopic, the crucible containing the residue after ignition should be kept covered with a closely fitting lid, from the time it is taken from the desiccator until the weight has been taken. Failure to take this precaution leads to entirely incorrect results. For the same reason exactly 0.400 gm. of this residue should not be taken for titration, as directed, but the entire quantity used.

MAGNESII OXIDUM.—The official statement that this forms a gelatinous mass with 15 parts of water does not apply to the products of this market. The comments under *Magnesii Carbonas* apply also to the oxide.

MANGANI SULPHAS.—In the test for alkalis and magnesium a residue of about 0.2 percent. should be allowed. In the test for zinc, ferric compounds, present in permissible quantity, may cause precipitation of sulphur, which may be mistaken for zinc sulphide. The test is better made by adding hydrogen sulphide to the filtrate from the precipitate produced by an excess of ammonium carbonate in a water-solution of the salt previously treated with chlorine.

METHYLIS SALICYLAS.—The alkaline liquid (last paragraph) should be heated at 100° C. for at least 5 minutes, to saponify the ester, before it is diluted with water, otherwise most of the methyl salicylate will be precipitated unchanged by the hydrochloric acid.

METHYLTHIONINAE HYDROCHLORIDUM.—The U. S. P. is in error in assigning an anhydrous formula to the crystalline compound; it contains 3 molecules (=14.46 percent.) of water, of which it loses two at 100°, the remainder at 150°. The ash requirement is too stringent, as few obtainable specimens come within its limits; a maximum of 1 percent. has been proposed and can be readily met. As any zinc compounds present are likely to be reduced, at least partially, to

metal during incineration, and as zinc is volatile at comparatively low temperatures, this impurity may escape detection unless special precautions are taken. It is recommended that the test be carried out somewhat as follows: 0.5 gm. of sample is carbonized at a temperature below a red heat, in a porcelain crucible. The residue is powdered and boiled for 5 minutes with 10 cc. of diluted hydrochloric acid. The mixture is then filtered and the filter washed with 10 cc. of water. The combined liquids are boiled with 1 cc. of nitric acid, then supersaturated with ammonia water and filtered if not clear. Ammonium sulphide should produce no turbidity in the filtrate. The official test for arsenic is defective in that the proportions of potassium nitrate and sodium carbonate are not specified and in that the nitric acid is not eliminated before treatment with sulphurous acid. There seems also to be no good reason why the test should be four times as stringent as it is for most other official substances. The following is recommended to replace the present test: A powdered mixture of 0.5 gm. of sample and 1 gm. each of potassium nitrate and dried sodium carbonate is heated in a crucible until the organic matter is completely oxidized. The cooled residue is dissolved in 10 cc. of diluted sulphuric acid and the solution evaporated over a flame until sulphuric acid begins to vaporize. The residue should not respond to the Modified Gutzeit's Test (U. S. P. VIII). Adulteration with dextrin has been noted by J. M. Francis and C. E. Vanderkleed. It may be detected by its insolubility in alcohol; the amount of insoluble residue, obtained by boiling about 1 gm. of methylene blue with 50 cc. of alcohol, washing on a filter with 50 cc. of hot alcohol, and drying at 100°, might be limited to 1 percent.

MORPHINA.—A definite melting point cannot be stipulated, as the alkaloid decomposes below the melting temperature and then melts at temperatures varying with the rate of heating and other conditions. Residues on incineration should not exceed 0.05 percent.

MORPHINAE ACETAS.—It has more than a "faint" odor of acetic acid, owing to gradual spontaneous decomposition. Residues on incineration should not exceed 0.05 percent. The precipitate produced by ammonia water is nearly white only in case of a freshly made salt; older products yield buff-colored to light brown precipitates. The same applies to the color of solutions of the salt in aqueous caustic alkali. Because of its instability this salt cannot be expected to meet the U. S. P. requirements as to color and solubility, except when freshly made. Rapid deterioration and the generally conceded fact that it serves no purpose that is not served better by one of the other official morphine salts, make it desirable that the use of the acetate be stopped. Among 12 of the most important foreign pharmacopoeias only the British recognizes it. The Belgian, German, and Swiss pharmacopoeias either direct or permit substitution of the hydrochloride when the acetate is ordered.

MORPHINAE HYDROCHLORIDUM.—The following tests should be added. A water-solution of the salt (1 in 50), should not be rendered turbid by diluted sulphuric acid (barium) nor, when acidulated with hydrochloric acid, by barium chloride (sulphates).

PARAFFINUM.—The requirement that "its alcoholic solution should not redden moistened blue litmus paper" conflicts somewhat with the statement in the pre-

ceding paragraph that paraffin is insoluble in alcohol. The test is preferably made by shaking melted paraffin with an equal volume of hot water and testing the latter with litmus.

PARALDEHYDUM.—The chief impurities in this are acetaldehyde and, according to R. Richter, metaldehyde. Excessive quantities of these are shown by abnormal freezing and boiling points. The official statements that paraldehyde solidifies “when cooled to near 0°C,” and “becomes liquid again at 10.5° C,” may occasion rejection of the best products of the market. The German Pharmacopoeia states that paraldehyde containing about 4 percent. of acetaldehyde congeals at 6° to 7°, but gives no melting point. The experience of this laboratory is that specimens which have approximately the official boiling point congeal at practically the same temperatures at which they melt, usually 8° or 9° C. The melting point 10.5° of the U. S. P. is a figure given by some authorities for the chemically pure substance and is not likely to be reached by medicinal products. The official figures should probably be changed to a requirement that the congealing point be not lower than 6°. The melting point is superfluous as a test of purity. The specific gravities of specimens of good quality tested of late ranged from 0.9910 to 0.9928 at 25°, all of them being higher than the official figures. It is recommended that the specific gravity be given as “about 0.992 at 25°,” but not required as a test of purity.

PELLETIERINAE TANNAS.—The products of the market differ more or less from the preparation described in the U. S. P. They are usually incompletely soluble in water and in alcohol and the prescribed color tests are inadequate, as the reactions are obscured by the tannin or other organic matter. On extraction of the alkaloids by shaking with chloroform and caustic alkali solution, acidulating the chloroform extracts with hydrochloric acid, then evaporating and drying, residues of 17 to 20 percent. of alkaloid chlorides have been obtained. These residues responded readily to the selenous acid test and produced only light yellow colors with sulphuric or nitric acid.

PHENOL.—The required minimum contents of actual phenol might be raised to 98 percent., as that strength, rather than 96 percent., corresponds to the official congealing point limits of 39°. Determination of the congealing point is one of the most important of the tests; it makes a quantitative determination of phenol, as well as the glycerin test and a boiling point determination practically superfluous. The stated solubility in water is wrong; it should be about “12” instead of “19.6” parts.

PHENOL LIQUEFACTUM.—Products obtained by the official method contain at least 88 and may contain up to 90 percent. of actual phenol; some such range would be preferable to the present minimum of 86.4 percent. The official congealing point, 13.5°, corresponds to about 88 percent. of phenol. In connection with the boiling point, “188°” should be changed to “182°.”

PHENYLIS SALICYLAS.—The melting point is an important test of purity, but the rigid figure 42° should give way to a range of about 41° to 43°, within which limits the melting interval should be required to fall.

PHOSPHORUS.—Specific gravity and melting point are not required either for identification or as criteria of purity and as these constants, as given in the U. S.

P., are those of entirely pure phosphorus, they are inapplicable to medicinal-commercial products and can be considered merely as informative statements, not as requirements. Phosphorus is not as soluble in chloroform as officially stated, but requires about 40 parts of the solvent.

PHYSOSTIGMINAE SALICYLAS.—Determination of the melting point is too uncertain in its results, because of partial decomposition, to be of much value as a test of purity. The salt is officially described as having an acid reaction to litmus, but this is not always true of the market product, which is sometimes neutral. Because of its use in eye-drops, more than traces of acid are probably objectionable and it might be well if it were required to be neutral or not more than faintly acid to litmus paper when tested in a cold-saturated water-solution. For distinguishing this salt from the sulphate, the indirect test with platonic chloride is inconclusive and unreliable; it is sufficiently well identified as a salicylate by the ferric chloride test and presence of sulphate is more conclusively shown with barium chloride.

PHYSOSTIGMINAE SULPHAS.—Remarks under the preceding apply also to this salt. The test for excessive acidity should be made in a 1-20 solution. The statement that this salt "yields only a faint yellow color" with sulphuric acid is correct only when the proportion of the former is exceedingly small, but as a test for easily carbonizable impurities a solution of 0.1 gm. in 2 cc. of the acid should not become darker than yellow within 5 minutes.

PILOCARPINAE HYDROCHLORIDUM.—Different authorities give melting points ranging from 193° to 205°; variations of 195° to 198° have been noted in this laboratory. This uncertainty about the melting point lessens its value as a test for excessive contamination with other Pilocarpus alkaloids or decomposition products. Determination of optical rotation may prove more satisfactory; the French Pharmacopoeia states that the specific rotatory power is $^{\alpha}D_{18}^{\circ} = +91^{\circ}$, when determined in a water-solution containing 2 gm. of the salt in 100 cc.

PILOCARPINAE NITRAS.—To exclude excessive quantities of other Pilocarpus alkaloids, etc., the *British Pharmaceutical Codex* proposes that the melting point should not be lower than 172° C. The pure salt is generally considered to melt at 177° to 178°. Specific rotatory power according to the French Pharmacopoeia, is $^{\alpha}D_{18}^{\circ} = 82.2^{\circ}$.

PLUMBI ACETAS.—Market products do not conform strictly to the official specifications, being sufficiently basic to cause them to contain less than the required minimum of 99.5 percent. of the crystallized normal salt. A. Seidell found the lead in a number of samples to correspond to 101.6 to 106.1 percent. of $Pb(C_2H_3O_2)_2 \cdot 3H_2O$. A strictly normal salt would not be acceptable to the drug trade because of its strong odor of acetic acid and its instability. However, this varying basicity should be kept within reasonable limits and it is therefore recommended that the salt should contain a quantity of lead corresponding to not less than 99.5 nor more than 105 percent. of $Pb(C_2H_3O_2)_2 \cdot 3H_2O$. Solutions (1 in 20) in water are usually more than "slightly" alkaline to litmus. The allowable limits of foreign metals, etc. should be more clearly defined than by terms like "slight precipitate" and "slight residue."

POTASSII ACETAS.—The salt must be dried for at least 2 hours at 150° to render it anhydrous before assaying. In determinations of the type involved in the assay of this salt, the washings of the charred mass should be tested for alkalinity with litmus or phenolphthalein, not with methyl-orange as directed. This error occurs also in connection with the assays of other official alkali salts of organic acids. It is also advisable to boil the mass with water for 15 minutes or longer to facilitate extraction, preferably in platinum, as all except the most resistant glass may increase the alkalinity of the liquid sufficiently to introduce a serious error. An alternative method, which has been found satisfactory in this laboratory, consists in boiling the charred mass with an excess of volumetric sulphuric acid, filtering, washing and titrating the excess of acid.

POTASSII BICARBONAS.—The stated percentage of loss in weight at red heat and the statement that concentrated solutions in water are neutral to phenolphthalein are not to be understood as specifications for the medicinal salt, but merely as characteristics of the chemically pure substance.

POTASSII BITARTRAS.—A minimum standard of 99 percent. is unnecessarily low, and might be raised to 99.5 percent., the commercial product being frequently 99.9 percent. pure. For the test for alum and phosphates the mixture with potassium carbonate and nitrate should not be heated in a porcelain crucible, as officially directed, but in platinum. An assay is made more conveniently than by the official method, and with less risk of error by direct titration of a water-solution of 0.8 to 0.9 gm. of the salt with N/10 alkali with phenolphthalein as indicator.

POTASSII BROMIDUM.—The product of representative manufacturers is now at least 98.5 percent. pure, the chief impurity being potassium chloride, and the standard could be raised to that figure. The indirect quantitative determination of the mixed bromide and chloride by titration with silver nitrate is liable to be rendered grossly inaccurate by potassium sulphate, which may be present in considerable quantity in a carelessly made salt and for which no test is now required; not more than slight traces of sulphate should be allowed. It would also be a simple matter for unscrupulous persons to add to a product containing an excessive amount of chloride enough potassium sulphate to bring the amount of silver nitrate required for precipitation within the specified limits. Such mixtures would stand the other official tests also.

POTASSII CARBONAS.—To remove water completely in a reasonable length of time, a temperature of 150° to 160° is required.

POTASSII CHLORAS.—The impurities in this salt, as found in the market, are usually present only in traces. Quantitative determinations are therefore superfluous, as a rule, and the present standard of 99 percent. can be raised to 99.5 percent.

POTASSII CITRAS.—See comments under *Potassii Acetas* concerning the assay.

POTASSII CYANIDUM.—Potassium cyanide of U. S. P. standard is practically unobtainable. Sodium cyanide and mixtures of sodium and potassium cyanides containing the amount of cyanogen required in the official salt, however, are available.

POTASSII HYPOPHOSPHIS.—A new method, by Rupp and Kroll, for the determination of hypophosphorous acid in calcium hypophosphite, recently published (*Archiv d. Pharm.*, v. 249, pp. 493-7), is likely to prove more reliable and convenient than any other known at this time for the assay of most of the official hypophosphites. It consists in oxidation with an excess of Koppeschaar's solution according to the equation: $\text{H}_3\text{PO}_2 + 4\text{Br} + 2\text{H}_2\text{O} = \text{H}_3\text{PO}_4 + 4\text{HBr}$. The procedure is like that for the determination of phenol. The accuracy of the method has been verified by at least one investigator, who makes the only objection that phosphites, if present, raise the result. The amount of this impurity in a purified salt, however, is not likely to be sufficient to exert an appreciable influence on the results. No tests for phosphites in hypophosphites are given in the U. S. P. That of the German Pharmacopoeia for phosphite and phosphate, requiring that a water-solution (1+19) of calcium hypophosphite, acidulated with acetic acid, should not be rendered turbid at once by lead acetate, is applicable also to the alkali hypophosphites.

POTASSII IODIDUM.—The official method of titration of iodides is not satisfactory, as it requires considerable practice to obtain accurate results, because of uncertainty of the end point; more reliable results have been obtained with Volhard's method. A test for sulphates should be added, as these may be present in a carelessly made salt and cause the percentage of actual potassium iodide, as determined by titration with silver nitrate, to appear higher than it is, provided the salt also contains the usual amount of potassium chloride. For the titration, samples should be powdered and dried a few hours at 100° to 110° C. before weighing.

POTASSII NITRAS.—If a dried specimen of this salt, containing not more than 3 percent. of moisture, shows presence of less than 1 percent. of potassium chloride by titration with silver nitrate and of not more than traces of sodium by the flame test, and in addition stands the U. S. P. tests for impurities, it may safely be considered to comply with the minimum standard of 99 percent. If more than a trace of sodium be found, a determination of potassium would logically be required and in doubtful cases also a determination of nitric acid, to settle the question. A melting point of exactly 353° should not be regarded as a requirement. Authorities are by no means unanimous about the melting point of the chemically pure salt, much less about a salt containing up to 1 percent. of impurities.

POTASSII PERMANGANAS.—The directions fail to state, in connection with the assay, that the mixture should be warmed until clear and colorless before determination of the excess of oxalic acid.

PYROGALLOL.—It is recommended that in place of the present melting point a melting interval, with limits from 130° to 133°, be required and that presence of not more than 0.05 percent. of non-volatile matter be allowed. While it is possible to make solutions so weak that they will comply literally with the specification that "the freshly prepared aqueous solution is neutral to litmus paper and colorless," a common sense construction of the statement would require that a solution of the strength most generally used for U. S. P. tests of purity, namely 5 percent., be examined. Solutions of this strength, of the best obtainable pro-

ducts, in freshly boiled and cooled distilled water, are invariably slightly acid and yellowish, the depth of color, of course, varying with the bulk examined. The specifications should be changed accordingly.

PYROXYLINUM.—A limit of 0.2 to 0.3 percent. of mineral impurities should be allowed and it is important that a test for acids be added. A test to limit moisture has been suggested to be desirable.

QUININA.—The melting points of quinine and its compounds of medicinal purity must necessarily vary within rather wide limits, since varying amounts of cinchonidine, hydroquinine, etc., are always present. As these constants are not needed for establishing identity or purity, they should either be omitted or stated to apply to the chemically pure substances only. The thalleoquin reaction cannot be obtained by following the official directions, the amount of bromine being entirely too large; not more than 1 or 2 drops of the official test solution should be used. The details of this test have apparently been adjusted as a result of trials with bromine water that had lost the greater part of its bromine. Such deterioration is almost certain with bromine water made by the official directions. It is preferable, if it is to be kept for any length of time, to make the solution with an excess of bromine, so that the water will always be nearly saturated with bromine regardless of loss by evaporation or chemical change. Solubility of quinine in a mixture of absolute alcohol and ether is incapable of showing "absence" of cinchonine and cinchonidine, moreover, presence of a limited amount of other Cinchona alkaloids, chief of which is cinchonidine, is allowed by another test. The color of the solution obtained in the sulphuric acid test for readily carbonizable matter is affected by the relative and absolute quantities of quinine and of the acid taken; a solution of 0.1 gm. of quinine in 2 cc. of sulphuric acid should not be darker than light yellow. In the test for ammonium compounds the quantity of reagent is given but not that of the quinine; mere traces of ammonium salts are legitimate, unobjectionable impurities and if more than 0.2 gm. of quinine is taken for the test, it is unnecessarily severe. Quinine should not yield more than 0.1 percent. of ash. As regards the ammonia test for other Cinchona alkaloids, the inconsistency of disregarding the proportion of alkaloid in the several official quinine compounds has been pointed out by A. B. Prescott, A. B. Lyons, and others. To remedy this defect, it would seem best to leave the test unchanged in the form it is now given under *Quininae Sulphas*, but in every other case direct to take such an amount of the compound in question as will contain the same weight of alkaloid as does 1.8 gm. of quinine sulphate that has been dried at 50° and then contains 2 molecules of water. In case of quinine, 1.74 gm. of the trihydrate would be the amount required, instead of 2 gm., weighed after drying at 50° for 2 hours. The directions for indiscriminate drying at 50° of various quinine compounds for this test are without any good reason so far discovered; this procedure makes still more disproportionate the relative stringency of the test as applied to the several compounds. As the test is based on results with quinine sulphate having a neutral or only slightly alkaline reaction to litmus, the use of hematoxylin as indicator for the neutralization of quinine is questionable, since there is evidence that the neutral points obtained with this indicator and with litmus do not coincide. Litmus solution properly made from ma-

terial of good quality is sufficiently sensitive, if the alcohol-solution of quinine is diluted with about twice its volume of water, but neither litmus nor hematoxylin is sensitive enough in strongly alcoholic mixtures for accurate neutralization of most alkaloids. It is recommended to change the official test as follows: Dissolve 1.74 gm. of quinine in 20 cc. of alcohol, dilute the solution with 50 cc. of hot water and neutralize it with normal sulphuric acid, using litmus T. S. as indicator. Evaporate the liquid to dryness in a porcelain dish on a water-bath, powder the residue, and mix it in a test-tube with 20 cc. of water. Complete the test as directed under *Quininae Sulphas*.

QUININAE BISULPHAS.—In view of the fact, which has been recognized by the Italian Pharmacopoeia, that the solubility of quinine sulphate in water is influenced by the presence of metallic salts, such as sodium sulphate, chloride, etc., it is advisable to avoid introduction of such salts in the application of the ammonia test for other Cinchona alkaloids to quinine compounds; it is preferable to separate the free alkaloids by a shaking-out process, then proceed as recommended above under *Quinina*. In place of 2 gm. of a salt that has been dried for 2 hours at 50°, 2.52 gm. of the crystallized salt should be taken for this test. For further comments see under *Quinina*.

QUININAE HYDROBROMIDUM.—In the nitric acid test for morphine, an orange color is produced, due to liberation of bromine, but no deep red color, fading to orange, should be noticeable. As barium salts are used by manufacturers to remove sulphates from the salt, addition of a few drops of diluted sulphuric acid to 10 cc. of a hot water-solution (1 in 50) of the salt should cause no turbidity. In place of 3 gm. of a salt that has been dried for two hours at 50°, 2.93 gm. of the crystallized salt should be taken for the test for other Cinchona alkaloids, if 30 cc. of water are to be taken for the final maceration, or two-thirds of that quantity if 20 cc. of water are to be used. For further comments see under *Quinina* and *Quininae Bisulphas*.

QUININAE HYDROCHLORIDUM.—A test for barium should be added for reasons stated under *Quininae Hydrobromidum*. In place of 3 gm. of a salt that has been dried for 2 hours at 50°, 2.75 gm. of the crystallized salt should be taken for the test for other Cinchona alkaloids, if 30 cc. of water are to be taken for the final maceration, or two-thirds of that quantity if 20 cc. of water are to be taken. For further comments see under *Quinina* and *Quininae Bisulphas*.

QUININAE SALICYLAS.—The figures of the U. S. P. for solubility in water and alcohol are incorrect; A. Seidell found the salt soluble in about 1500 parts water and in about 21 parts of alcohol. The formula of the salt as found in the market is not as given in the U. S. P. but is $C_{20}H_{24}O_2N_2 \cdot C_7H_6O_3 \cdot H_2O$, which corresponds to 3.78 percent. of crystal-water; the limit of loss at 100°, therefore, is placed more properly at about 4, rather than 2 percent. Tests for absence of more than traces of chlorides and sulphates might be added to advantage. In place of 2 gm., 2.21 gm. of the salt should be taken for the test for other Cinchona alkaloids, about 5 cc. of ammonia water should be used in the shaking-out process, and the alcohol-solution of alkaloids should be diluted with about 50 cc. of hot water, to render the indicator (litmus solution) more sensitive. For further comments see under *Quinina*.

QUININAE SULPHAS.—Solutions in water are usually slightly alkaline to litmus. It is advisable, in making the test for other cinchona alkaloids, to choose a water-bath of considerable size for the macerations, so that an even temperature can be maintained more readily. There is no reason for deviating 1 or 2 degrees from the specified temperatures and the portion of the official text allowing this is better omitted, as it is likely to lead to careless manipulation. For further comments see under *Quinina*.

(To be continued.)

INTERNATIONAL STANDARDS FOR COLORED FLUIDS.*

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Introduction: That the color of certain fluids is a distinct factor in pure chemistry is evident from the employment of such colorimetric tests as that of Wessler, and when we turn to applied chemistry, we find the color of liquid products of such esthetic influence to the consumer as to be of vital commercial value to the manufacturer. This is the philosophy of use of coloring agents in pharmacy and furthermore explains the call for uniformity in the tint of natural colored products. So it is that manufacturers of oils, beer and whiskey seek uniformity in color of their products by the use of colorimeters; that is why Professor Felix Ehrlich (*Zeitschrift Ver. Zuckerind* 59) (1909) (746) has advocated international standardization of caramel by use of the definite brown substance, *Saccharan*, which he prepared from sugar. Professor Ehrlich's effort to establish an international standard for caramel is the partial expression of a still broader need of international uniformity of colors, this need being fittingly expressed by Hans Moeller at the International Pharmaceutical Congress of 1910 (*Berichte der Deutschen Pharmazeutischen Gesellschaft*, 10, 1910, 358), as follows:

“Ein neues Gebiet, auf dem—meiner Meinung nach—jetzt internationale Regeln fest gesetzt werden solten is zweifelsohn das der exakten Farben bestimmungen.”

The subject was brought to the writer in his capacity as member of the Committee on Revision of the National Formulary, there being entrusted to a subcommittee of which he was a member, the problem of standardizing tincture of caramel (*Saccharum ustum*) and tincture of cudbear (*Persionis*) which is proposed to recognize in the forthcoming edition of that work. It is needless to repeat the numerous and practically fruitless efforts toward standardization already reported by the writer (*American Druggist* 59, 1912, 35) except to say that while some of the plans tried out were satisfactory, each possessed the in-

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