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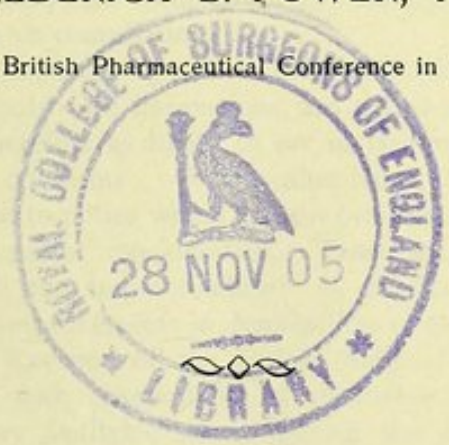
SOME OBSERVATIONS AND SUGGESTIONS RELATING TO THE CHEMISTRY OF THE BRITISH PHARMACOPOEIA

BY

FREDERICK B. POWER, PH.D.

[Read before the British Pharmaceutical Conference in London, July, 1900]



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SOME OBSERVATIONS AND SUGGESTIONS RELATING TO THE CHEMISTRY OF THE BRITISH PHARMACOPŒIA*

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THE appearance of a new national Pharmacopœia is always an event of considerable interest, for it may reasonably be assumed that it will reflect, so far as is practicable in a work of that character, the progress in the sciences relating to pharmacy and medicine during the period that has elapsed since its last preceding revision. The importance of a new edition of such a work is manifest when it is considered how large a circle it concerns, inasmuch as it is designed to represent a standard to which medical men, pharmacists, public analysts, and chemical or pharmaceutical manufacturers are expected to conform.

It is therefore natural, and, indeed, desirable, that the appearance of a new national Pharmacopœia should be attended by some expressions of opinion on the part of those who are interested in it, and whose work, to a greater or less extent, is affected by it; for even a work that is issued *By Authority* can hardly be expected to be perfectly free from errors and defects, however much care may have been bestowed on its compilation.

The comments that immediately follow the publication of such a work, in so far as they represent only first impressions, are apt to be somewhat superficial in their character, and therefore as likely to err in bestowing unqualified praise as in the severity of the criticisms. On the other hand, there are also from time to time some facts brought to notice which possess positive and lasting value, and are therefore worthy of careful consideration. These may relate either to actual errors in the text, to the impracticability of particular requirements, or to suggestions for further improvements in descriptions or processes.

The Committee of Revision of the United States Pharmacopœia have long recognised the value of such observations or criticisms, and have taken pains to collate them from every available source during the intervals of the last two revisions, or for a period of nearly twenty years. Under the title, "Digest of Criticisms," they have been published and issued gratuitously by the Committee to the medical and pharmaceutical societies and colleges immediately concerned, and to all those, either at home or abroad, who were supposed to be specially interested in the work. It will be evident that by the adoption of this plan considerable aid is given to those upon whom the preparation of a subsequent edition of the United States Pharmacopœia depends, even though but a comparatively small part of the collected material may be eventually utilised.

Although the chemistry of the British Pharmacopœia has already received some consideration at the hands of the critics,† the published papers and discussions relating thereto have been somewhat fragmentary, and no attempt appears to have been made to subject it to a more complete and systematic review.

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* Read before the British Pharmaceutical Conference, London, July, 1900.

† 'Year Book of Pharmacy,' 1898, pp. 452, 456, 467; *Pharmaceutical Journal*, 1898, **60**, p. 394, **61**, pp. 666, 684; *Chemist and Druggist*, 1898, **52**, p. 674, **53**, p. 348; *British and Colonial Druggist*, 1898, **33**, p. 515 **34**, pp. 107, 515, 719; 1899, **35**, p. 160.

More than two years have now elapsed since the appearance of the work, and it has therefore seemed desirable to indicate some errors which appear to have escaped notice, or to which at least attention has not yet been directed. In addition to these, it has been thought useful to incorporate references to some previously published observations, either for the purpose of further confirming them or for other comments, as also for the sake of completeness. It may likewise be stated that the criticisms made by the writer relating to the officially described characters or tests of individual chemicals have been, so far as possible, substantiated by experiment, even in cases where incorrectness of statement has been so obvious as seemingly not to require it. By the inclusion of such experimental work it has been the aim to impart to the criticisms a constructive character.

It is in this broad spirit, but entirely on his own initiative and responsibility, that the writer has undertaken to present the following observations on the chemistry of the British Pharmacopœia, and it is hoped that they may contribute in some degree to its perfection and usefulness.

Acetanilide.

The text of this chemical, which is first in the list of the Pharmacopœia,* contains some errors of a particularly interesting character. It is stated, for example, that "on boiling with *test-solution of ferric chloride* a reddish-brown colour is produced, and this is almost entirely discharged by hydrochloric acid." The well-known fact appears to have been overlooked that test-solution of ferric chloride alone becomes reddish-brown on boiling, owing to the formation of a basic salt, although if the solution is sufficiently dilute it may remain perfectly clear (compare Schmidt, 'Pharm. Chemie,' 3rd edit., vol. i., p. 764). The Swiss Pharmacopœia (*editio tertia*), 1893, strangely enough, contains the same error, since it states: "The aqueous solution of antifebrin affords on boiling with a few drops of ferric chloride a dark brown-red colour, and on the addition of hydrochloric acid again becomes pale yellow." If this test be made with a cold saturated aqueous solution of antifebrin, and also with distilled water to which the same amount of solution of ferric chloride has been added, there is practically no difference whatever in the shade of colour of the two liquids after boiling, and precisely the same yellow colour is produced in both on the subsequent addition of hydrochloric acid. The conclusion must be that this test has been formulated by someone who was not familiar with the change of colour produced in a solution of ferric chloride on boiling. In this connection attention may also be called to the official *test-solution of ferric chloride*, p. 415, which is directed to be made from *commercial anhydrous* ferric chloride. The questions arise whether there is any anhydrous ferric chloride except the commercial, and, furthermore, whether the anhydrous salt is really intended to be used. The ordinary commercial ferric chloride, occurring in crystalline masses, is, of course, not anhydrous, but has the composition $Fe_2Cl_6 \cdot 12H_2O$. In ordering the anhydrous salt from one of the large London dealers in chemicals, the writer was informed that it would be necessary to send to the Continent for it. It is also not obvious what advantage there can be in the use of the anhydrous salt for the purpose of a test solution of ferric chloride, as it requires to be dissolved in water, and it costs about ten times the price of the ordinary crystallised salt.

Another most peculiar error in the text for acetanilide is included in the following statement:—"A cold saturated aqueous solution . . . . is not affected by test-solution of ferric chloride (absence of *acetone*, etc.)." It would be

* Whenever in the following notes the Pharmacopœia is cited, the British Pharmacopœia is intended.

somewhat surprising in the first place if dry, crystallised acetanilide should be capable of containing as an impurity such a very volatile liquid as acetone, for experiment has shown that even when crystallised from the latter it does not combine with it, and furthermore acetone gives no very specific reaction with ferric chloride. A cold saturated aqueous solution of acetanilide which had been freshly crystallised from acetone was prepared, and, as was to be expected, this was no more affected by ferric chloride than an equal volume of distilled water, and even considerable acetone may be added to such a solution without any visible change. In fact, pure acetone gives but a faint yellowish colour with ferric chloride, not at all comparable in intensity, for example, to the colour afforded by absolute alcohol. This test for acetone appears, moreover, to be based upon a misinterpretation of Gerhardt's test for the detection of acetone in urine (see also *Pharm. Journ.*, April 1899, p. 387). It does not really detect acetone, or, at least, only indirectly, but rather the so-called ethyl diacetic acid, now known as ethyl acetoacetate, $C_6H_{10}O_3$ or $CH_3—CO—CH_2—CO_2C_2H_5$, which gives a purple colour with ferric chloride. Thus it is stated in Neubauer and Vogel's 'Analysis of the Urine,' American, from the seventh German edition, New York, 1879, p. 158, "Gerhardt first laid stress on the fact that a diabetic urine in which acetone is contained or *formed* is at the same time characterised by a remarkable reaction, namely, treated with ferric chloride, a deep red-brown colour is produced. This reaction corresponds with the demeanour of ethyl diacetic acid discovered by Geuther, *which decomposes with great readiness into acetone*, alcohol and carbonic acid."

For some remarks on the detection of *phenacetin* in acetanilide see *Pharm. Journ.*, April, 1899, pp. 367, 402.

Glacial Acetic Acid.

Mr. J. C. Umney (*Pharm. Journ.*, August, 1898, p. 242, and January, 1900, p. 8) has noted a discrepancy between the required strength and the melting point of this acid.

Arsenious Acid.

Although from long usuage the title *acidum arseniosum* (arsenious acid) may not be considered incorrect, the writer would prefer that of *acidum arsenosum* (arsenous acid), as adopted by the U.S. Pharmacopœia, and which corresponds to the analogous phosphorous acid. It would also conform with the change in nomenclature adopted by the Pharmacopœia from sodium arseniate to sodium arsenate (*sodii arsenas*), and from ferri arsenias to *ferri arsenas*.

Benzoic Acid.

This is stated to be "obtained from benzoin by sublimation," but it is also obtained from benzoin, and probably much more largely, in the wet way, by the lime method. It is probably not intended to exclude the latter product, since the Pharmacopœia permits the acid to be obtained from toluene and other compounds. The German and Swiss Pharmacopœias restrict the benzoic acid to that obtained from benzoin by sublimation, whereas the French Codex, under a distinct title, also recognises that prepared from benzoin in the wet way.

Boric Acid.

The synonym, *hydrogen borate*, has been criticised as being somewhat out of place in a Pharmacopœia, especially as no corresponding synonym is given for any of the other acids. The statement that "boric acid *liquefies when warmed*, and on *careful heating* loses 43.6 per cent. of its weight," is extremely vague, and gives a very incorrect idea of its behaviour. As stated in the U.S. Pharmacopœia and in chemical text-books, and as more recently noted by E. Merck (*Chemist and*

Druggist, August, 1898, p. 349), when boric acid is heated to 100° C. it is converted into metaboric acid, HBO_2, which slowly volatilises at that temperature. The metaboric acid fuses at 160° C., by prolonged heating at the latter temperature tetraboric acid, $H_2B_4O_7$, is formed, and it is only by strong ignition that boron trioxide or sesquioxide, B_2O_3, is obtained, which is the compound corresponding to the loss of weight indicated by the Pharmacopœia as produced on careful heating.

Citric Acid.

David Howard (*Chemist and Druggist*, April 1898, page 675) has called attention to the unsatisfactory character of the Pharmacopœia tests for lead in citric and tartaric acids. He notes that by requiring the acid to be neutralised with solution of ammonia, if the exact point of neutrality is passed, a dark coloration with hydrogen sulphide may be caused by the presence of traces of iron as well as of *lead*. The United States, German and Swiss Pharmacopœias avoid the possibility of such a mistake by directing the acid to be only partially or approximately neutralised with ammonia.

Gallic Acid.

The Pharmacopœia states that the aqueous solution of this acid is not precipitated by *tartarated antimony* (showing absence of tannic acid). This is an error which has previously been noticed by both Dr. Sillar and D. B. Dott (*Pharm. Journ.*, Dec., 1898, p. 684, and Jan., 1899, p. 58), and it is somewhat strange that it should also appear in the Swiss Pharmacopœia. If, for example, to 1 C.c. of an aqueous solution of gallic acid 5 C.c. of a saturated aqueous solution of tartarated antimony be added, a white precipitate is soon formed, and the filtered liquid then affords but a very slight reaction with ferric chloride, thus proving that the gallic acid is quite completely precipitated. The above incorrect statement has also been copied into Hager's 'Handbuch.' Beilstein ('Handbuch der organischen Chemie,' Bd. ii., p. 1920) mentions a gallate of antimony, of uncertain composition, as an *insoluble precipitate*.

Hydrobromic Acid.

A new and most excellent method for preparing this acid in a pure state has recently been published by Dr. A. Scott, F.R.S. (*Jour. Chem. Soc.*, 1900, p. 648).

Phosphoric Acid.

The Pharmacopœia states that this "may be prepared by treating with water and nitric acid *the residue left after burning phosphorus in air*." This is not quite correctly expressed, since it is not the *residue* left after burning phosphorus, but the *product of its combustion* in the air, from which phosphoric acid may be prepared.

Salicylic Acid.

The Pharmacopœia states that the crystals "below 392° F. (200° C.) volatilise without decomposition." This might be made a little more exact, as salicylic acid sublimes slowly at the temperature of a water bath (about 100° C.).

Sulphuric Acid.

Schlagdenhauffen and Pagel (*Apoth. Zeit.* 1900, No. 36, p. 302, from *Journ. de Pharm. et de Chim.*) have recently noted the frequent occurrence of *selenium* in sulphuric acid, as out of twelve samples supplied as "chemically pure" only three were found to be free from this contamination. They identified it by means of Dragendorff's codeine reaction, which consists in bringing a little codeine in contact with five or six drops of sulphuric acid containing selenium, when at ordinary temperatures the liquid soon assumes a green colour. This reaction is of

interest, as codeine is stated to form a colourless solution with sulphuric acid, and it does so when the latter is pure, but, as stated in Fluckiger's 'Reactions' (English translation), p. 38, "frequently the reaction fails and the acid turns somewhat green. The frequent occurrence of selenium in the acid would appear to explain this result. In two samples of English acid tested by the writer this reaction was not obtained, a chemically pure acid giving a colourless solution with codeine, and a so-called commercial acid producing only a faint rose-tint.

Tannic Acid.

Under this title the Pharmacopœia makes the following remarkable statement :— "Tannic acid, $C_{14}H_{10}O_9$, $2H_2O$, may be extracted by water-saturated ether from galls *which have been subjected to a special fermentation.*" In the first place it seemed very strange to the writer that tannic acid should contain two molecules or any definite amount of water, considering the method of its preparation. In order to ascertain what authority there could be for such a statement, a search was made through the literature, including such standard works as Beilstein's 'Handbuch der org. Chemie,' Thorpe's 'Dictionary of Applied Chemistry,' Husemann's 'Die Planzenstoffe,' both Schmidt and Flückiger's 'Pharm. Chemie,' and a number of others, but in all of these the formula is given simply as $C_{14}H_{10}O_9$, and no mention whatever is made of any combined water. It was only in Richter's 'Organic Chemistry,' vol. ii. p. 231, that its formula with two molecules of water could be found. The statement is obviously incorrect, and the only explanation that appears at all probable is that the Pharmacopœia authorities have confused tannic acid with the β-digallic acid of Böttinger, which has been assigned the formula $C_{14}H_{10}O_9 + 2H_2O$ (compare Beilstein's 'Handbuch der org. Chemie, Bd. ii., p. 1925, and Berichte des Deutsch. Chem. Ges., 17, p. 1476). Böttinger expressly stated, however, that this substance, although resembling tannin, is not identical with it, inasmuch as on boiling with dilute sulphuric acid it is not converted into gallic acid. It was obtained by heating the ethyl ester of gallic acid with pyroracemic acid (or glyoxylic acid) and sulphuric acid. The α-digallic acid of Schiff (Beilstein, *loc. cit.*, p. 1924) was obtained by heating gallic acid with phosphorus oxychloride. It has the formula $C_{14}H_{10}O_9$, *contains no water*, and has all the properties of tannin.

The writer is also not aware that in the preparation of tannic acid the galls are "*subjected to a special fermentation.*" All the text-books at least indicate that the tannin is directly extracted from powdered galls by suitable solvents. On the other hand, it is well known that gallic acid may be prepared by the hydrolysis of tannic acid, and that this change may be effected by a ferment as well as by boiling with a dilute acid or alkali (compare Thorpe's 'Dictionary,' vol. iii., p. 775).

Aconitine.

As the Pharmacopœia aims to be conservative as well as authoritative, it seems somewhat questionable whether a formula should be assigned to this alkaloid, which even the author of it did not consider definitely established. In some Continental works, as, for example, in Hager's 'Handbuch,' Bd. i., p. 147, the slightly different formula of Freund, $C_{34}H_{47}NO_{11}$, seems to be preferred. (Compare also *Pharm. Journ.*, vol. lx., 1898, p. 394.)

The description, "colourless hexagonal prisms of the rhombic system," would appear to pertain to a specially prepared specimen, and not to the alkaloid as it occurs in commerce, which might be more correctly described as *in distinct crystals, or a crystalline powder*. The statement that "an alcoholic solution of the alkaloid turns the plane of a ray of polarised light to the right" (a somewhat cumbersome phrase for indicating that it is optically dextrogyrate) would seem to

be of very little value unless the degree of rotation is given, for it assures neither the identity nor the purity of the alkaloid.

Amyl Nitrite.

In the text of this article there occurs the following sentence:—"Submitted to distillation, about 70 per cent. passes over between 194° and 212° F. (90° and 100° C.), the bulb of the thermometer not dipping below the surface of the *residual fluid*." It is not clear why the word *residual* is inserted here, as the only residual fluid would be that portion remaining after distillation between the limits of temperature mentioned, when the thermometer is no longer required. The bulb of the thermometer should not at any time dip below the surface of the liquid.

Atropine.

For some comments on the Pharmacopœia text for atropine and atropine sulphate, as also for hyoscine hydrobromide and hyoscyamine sulphate, see "A Note on the Mydriatic Alkaloids," by Dr. H. A. D. Jowett (*Pharm. Journ.*, Aug. 1898, p. 195), and "Some New Gold Salts of Hyoscine, Hyoscyamine, and Atropine," by the same author (*Journ. Chem. Soc.*, 1897, p. 679).

Bismuth Carbonate.

In conformity with the official title of bismuth oxynitrate the title of this salt would be more correctly *bismuthi subcarbonas*. As it is so well known that the oxy salts of bismuth are not of constant composition, it seems quite inexplicable that the Pharmacopœia should assign to both the oxycarbonate and the oxynitrate definite formulas, and require them to yield amounts of bismuth sulphide exactly corresponding to these formulas. These thoroughly impractical requirements for the official bismuth preparations have been criticised by both David Howard and E. Merck (*Chemist and Druggist*, April 1898, p. 674, and Aug. 1898, p. 348). The official method of determining the bismuth in these compounds as sulphide is not one that commends itself, and E. Merck (*loc. cit.*) has given figures obtained by himself which prove that the determination as oxide is more accurate and reliable as well as very much more rapid. The absence of non-volatile impurities would, of course, be determined by the usual qualitative tests, and if these were present in any amount a quantitative determination of the bismuth would rarely be required. The variation in composition of these salts is apparent by a comparision of the requirements of some of the Pharmacopœias, as expressed in percentages of bismuth oxide.

Bismuth Subcarbonate.—B.P., 89.7 per cent.; U.S.P., 87-91 per cent.; Ph. Germ. Supp., at least 85 per cent. Bi_2O_3.

Bismuth Subnitrate.—B.P., 76.3 per cent.; U.S.P., 79-82 per cent.; Ph. Germ., 79-82 per cent.; Ph. Helv., about 80 per cent. Bi_2O_3. Compare also Thoms (*Apoth. Zeit.*, 1898, p. 318).

Bismuth Salicylate.

The Pharmacopœia text for this salt has already received considerable adverse criticism (see E. Merck, *Chemist and Druggist*, Aug. 1898, p. 348; D. Lloyd Howard, *Pharm. Journ.*, Aug. 1898, p. 233). The requirement that alcohol when shaken with the salt shall not give a violet colour with ferric chloride, can hardly have been based on actual observation. The writer has never seen a specimen of the salt, either as found in commerce or however carefully prepared, that would stand this test, and it cannot be expected that it should in view of the extreme facility with which these basic salts become dissociated. There is also an inconsistency in requiring that the salt shall yield very nearly the theoretical amount of bismuth sulphide—70 per cent. (theory requires 71 per cent.), whereas

a limit of 2 per cent. (62-64) is permitted in the more accurate determination as oxide. The theoretical amount of oxide is 64.3 per cent., but the salt is likely to be somewhat more basic, and therefore to afford a little higher percentage of oxide. Several commercial specimens examined by the writer have been found to afford 65-66 per cent. of bismuth oxide, and a very carefully prepared specimen gave 64.7 per cent. on ignition. It is difficult to harmonise the requirements that the salt should afford 62 to 64 per cent. of oxide, and at the same time give no reaction for free salicylic acid, when theoretically any smaller proportion of oxide than 64.3 per cent. would necessarily indicate the presence of a corresponding amount of free salicylic acid, assuming the absence of other impurities.

For the examination of bismuth salicylate it will usually be found sufficient, in connection with qualitative tests, to determine the amount of oxide afforded by ignition. Some methods have been proposed, however, which include the determination of the amount of salicylic acid in the salt, or are based upon the determination of the acid radical alone. It was thought of interest to compare the accuracy of these methods, and for this purpose one of the above-mentioned specimens of bismuth salicylate was employed, which afforded 64·7 per cent. of oxide on ignition.

(1) Kollo (*Proc. Amer. Pharm. Assoc.*, 1899, p. 719, from *Pharm. Post*, 1899) recommends heating the bismuth salicylate with a normal solution of potassium hydrate, collecting, drying, and weighing the bismuth hydroxide formed, and calculating it as oxide. The salicylic acid is determined in the filtrate and washings by titrating with normal hydrochloric acid, using phenolphthalein as an indicator.

(*a*) 1·9264 gramme of the salt treated in this manner gave of BiO(OH), dried at 95° C., 1·2710 gramme = 63·52 per cent. Bi_2O_3. This precipitate, however, after ignition, weighed 1·2390 gramme, corresponding to 64·33 per cent. Bi_2O_3. The filtrate from the bismuth hydroxide gave on titration a result indicating 40·8 per cent. $C_6H_4 \cdot OH \cdot COOH$.

(*b*) 1·8530 gramme of the salt gave 1·2095 gramme of bismuth hydroxide = 62·83 per cent. Bi_2O_3, and by titration of the filtrate 41·7 per cent. $C_6H_4 \cdot OH \cdot COOH$. The calculated amount of salicylic acid in the official compound is 38·45 per cent.

The above method cannot be considered satisfactory, as it involves sources of error. The low percentage of bismuth found when weighed as hydroxide appears to be due to the formation of a little oxide, as shown in (*a*), and the high percentage of salicylic acid, as ascertained by a blank experiment, is at least partially due to the absorption of carbon dioxide by the alkali during the operation of heating.

(2) Messinger and Vortmann (*Ber der deutsch. chem. Ges.*, **23**, p. 2,753) have proposed a method for determining salicylic acid which consists in precipitating it from its solution in an excess of alkali by decinormal iodine solution as diiodo-salicylic iodide, and, after acidulating and filtering, titrating the excess of iodine in the filtrate with thiosulphate. The reaction takes place as follows:—

$$C_6H_4(OH).COONa + 3NaOH + 3I_2 = C_6H_2I_2(OI)COONa + 3NaI + 3H_2O.$$

Fresenius and Grünhut (*Zeits. anal. Chem.*, **38**, p. 292) have criticised the method, but Messinger has more recently shown that under proper conditions it gives accurate results (*Journ. prakt. Chemie.*, **61**, p. 236, and *Chem. Centralb.*, Bd. i., 1900, p. 925). A trial of this method was conducted as follows:—0.4782 gramme of bismuth salicylate was dissolved in dilute hydrochloric acid, the bismuth precipitated by sodium hydrate, filtered, and the filtrate and washings made up to 250 C.c. 50 C.c. of this alkaline solution were brought into a 100 C.c. stoppered bottle, neutralised with sulphuric acid, and then 0.5 C.c. of a 10 per cent. solution

of sodium hydrate added. The bottle was then placed in a water bath at 60° C., and when warm 31 C.c. of N/10 iodine solution was added, and the bottle kept warm and shaken occasionally for a few minutes. When cool, the contents were acidulated with sulphuric acid, filtered into a flask, and the precipitate washed with a little water. The filtrate required 15.1 C.c. of N/10 sodium thiosulphate, showing that 15.9 C.c. of N/10 iodine solution had been absorbed. As 1 C.c. of the latter corresponds to 0.0023 gramme of salicylic acid, this indicates 38.25 per cent. of salicylic acid in the salt. A second titration of 50 C.c. of the filtrate gave precisely the same result. This is in quite close agreement with the calculated percentage of salicylic acid in the salt, 38.45 per cent., and the method may be considered a fairly accurate one. It is important that there should not be too large an excess of alkali used.

Borax.

E. Merck (*Chemist and Druggist*, Aug., 1898, p. 348) has criticised the requirements of the quantitative test as being too stringent.

Caffeine.

According to some recently published notes on caffeine, a question appears to have been raised respecting the correctness of the Pharmacopœia statement that "at 100° C. the crystals lose 8·49 per cent. of their weight," which corresponds to one molecule of water. David Howard (*Chemist and Druggist*, April, 1898, p. 675) remarks that "he has never known it to lose the last trace of hydration at that temperature." Tasilly (*Brit. and Col. Druggist*, March, 1899, p. 249, from *Bull. Soc. Chim.*) states that "hydrated caffeine, $C_8H_{10}N_4O_2 \cdot H_2O$, does not part with all its combined water, even when heated to 150° C., at which temperature caffeine begins to volatilise." The observation that caffeine loses its water of crystallisation at 100° C. is attributed to Strecker (Beilstein's 'Handbuch der org. Chemie,' Bd. iii., p. 957), and the writer believes it to be perfectly correct. The Pharmacopœia errs in its method of expression, as commercial caffeine probably never contains 8·49 per cent. of water, owing to the facility with which the crystals effloresce. It would therefore be more correct to simply state that "at 100° C. the crystals lose their water of crystallisation."

A sample of caffeine, freshly crystallised from water, and dried on bibulous paper, was heated for two hours at 100° C., and on subsequently heating for another half hour the weight was found to remain quite constant, thus indicating that all the water had been expelled. The loss in weight was 7·13 per cent., which corresponds to that found by Allen—namely, 7·05 and 7·10 per cent. (see Allen's 'Comm. Org. Analysis,' vol. iii., pt. ii., p. 475). Allen has thoroughly investigated this subject, and, as he remarks, it is probable that the deficiency is due to efflorescence, for the water of crystallisation is lost even by exposure over sulphuric acid at the ordinary temperature, so that it suffers no further loss of weight at 100° C. When heated to 120° C. it constantly loses weight, owing to slow volatilisation. It is obvious that with a freshly crystallised substance of this character it is impossible, when drying it in the air, to determine exactly when it has lost the last trace of adhering moisture, or, on the other hand, the point at which it begins to effloresce.

Caffeine Citrate.

The text of this article contains an error which also appears in the U.S. Pharmacopœia. This is that "with 3 parts of water it forms a clear, syrupy solution," whereas in reality it forms a stiff paste (see also *Proc. Amer. Pharm. Assoc.*, 1897, p. 714). If the mixture with three parts of water be gently warmed it forms a clear solution, but, on cooling, it again forms an almost solid mass of acicular crystals of cafleine. The Swiss Pharmacopœia states that the compound is "readily soluble in four parts of hot water," which is quite correct.

The Pharmacopœia further states:—"But more water (that is, more than three parts) dissociates the salt and affords a white precipitate of caffeine, which redissolves when *excess of water* is added." It would be somewhat strange if the compound should dissolve unchanged, as is implied, in exactly three parts of water, and that any further addition of water (how much "more water" is not stated) should dissociate it. It is quite well known, as the simplest experiment will prove, that the compound is dissociated as soon as it is brought in contact with water. If a little water be added to the warm solution, the caffeine separates out as a mass of acicular crystals, and not in a form which might be understood as a "white precipitate." This is said to "redissolve when *excess of water* is added"—an expression which does not seem to be very well chosen, and which is certainly not very precise.

Calcium Hypophosphite.

In the text of this article it is stated: "*Heated to redness the crystals ignite*, evolving spontaneously inflammable hydrogen phosphide, etc.," and a similar statement occurs in the 1885 Pharmacopœia. This sentence seems to present some confusion of ideas, for it is not really the crystals which ignite, but the gases evolved by their decomposition. As the text reads, it would appear as if spontaneously inflammable gases were evolved when the crystals ignite, which, of course, is not possible. A more correct statement of the decomposition is given under sodium hypophosphite. There are several points in the text of the hypophosphites, both in the British and the U.S. Pharmacopœias, which are in need of revision, and which have been very thoroughly considered in a paper by Dr. H. A. D. Jowett, entitled:—"The characters and methods of assay of the official hypophosphites" (*Pharm. Journ.*, Aug., 1898, p. 171).

Cerium Oxalate.

For an investigation of this salt, see a paper entitled "The composition and determination of Cerium Oxalate," by F. B. Power and Frank Shedden (*Journ. Soc. Chem. Ind.*, 1900, pp. 636-642).

Chloral Hydrate.

E. Merck (*Chemist and Druggist*, August 1898, p. 348) has noted that a solidifying point of fused chloral hydrate, such as that given by the Pharmacopœia, about 120° F. (48·9° C.) cannot be guaranteed, and that his own preparation solidifies at 44° C. The U.S. Pharmacopœia allows considerable latitude in giving the limits between 35° and 50° C.

Chloroform.

The Pharmacopœia states that "on allowing 20 C.c. to evaporate . . . . no foreign odour is perceptible *at any stage of the evaporation*." The directions for conducting this test are probably not intended to be followed literally, as they would require an amount of chloroform to be inhaled which would be somewhat unpleasant in its effects. The test of the U.S. Pharmacopœia seems, in this respect, to be more practical, and also quite adequate—namely, that when 20 C.c. of chloroform are evaporated as directed "no foreign odour should become perceptible *as the last portions disappear from the paper*, and the paper should be left nearly odourless when compared with a new, odourless filter."

Cocaine Hydrochloride.

There appears to be some doubt as to the correct melting point of this salt, but that given in the Pharmacopœia, 356° to 366·8° F. (180° to 186° C.), is evidently too low, and allows too much latitude. There is a superfluity of tests for identity. The important test with permanganate, as formulated by the

Pharmacopœia, is quite useless and practically devoid of meaning. It states: "A solution containing not less than 1 per cent. gives *with excess of solution of potassium permanganate a copious red precipitate which does not change colour within an hour.*" This test in order to be of any value requires to be conducted under very definite conditions, and not by observing the colour of the precipitate, but the colour of the liquid. The expression "*excess* of solution of potassium permanganate, if used without restriction, would seem to permit the use of any indefinite amount of the latter solution. It is also not apparent how any change of colour in the red precipitate (if it undergoes any change) can be observed in a solution containing an excess of permanganate. It will be found of interest in this connection to compare the very precise, but necessary conditions for the proper application of this test, as given in the United States, German, and Swiss Pharmacopœias.

The melting point of *cocaine* is stated by David Howard to be 98° C., and not 96°-98°, which would admit dangerous impurities (*Chemist and Druggist*, April, 1898, p. 675).

Codeine.

The following test of the Pharmacopœia for this alkaloid suggests some criticism. "*A saturated solution of codeine in water acidulated with hydrochloric acid* should give no blue colour, but only gradually a dull green, on the addition of test-solution of ferric chloride and a very dilute solution of potassium ferricyanide (absence of morphine *and other impurities*)." As the text reads, a *neutral* solution of codeine hydrochloride would be used in making this test, which would obviously be quite different in its character from the solution employed if a comma were placed after the word water, so as to read: "A saturated solution of codeine in water, acidulated with hydrochloric acid." Comparative experiments will show that the test is best conducted in the latter form, that is, in slightly *acid* solution. The statement that this test shows the absence of morphine "and other impurities" is certainly much too broad and most incorrect, for it will by no means detect all other impurities, as might be inferred, nor even any considerable proportion of possible impurities. Compare, for example, Flückiger's 'Reactions' (American edition, p. 76).

With respect to the solution of this alkaloid in sulphuric acid, reference may be made to the notes under the latter, and also to *Chemiker Zeitung* (*Repertorium*), 1897, pp. 80, 107.

Cotton.

Although cotton may not be considered a chemical preparation, the Pharmacopœia adops a chemical test for its identity, which is of considerable interest if not of special pharmaceutical importance. This test is expressed as follows: "It dissolves in concentrated solution of copper ammonio-sulphate." The U.S. Pharmacopœia of 1890 makes a similar statement—namely, "insoluble in ordinary solvents, but soluble in copper ammonium sulphate solution," which likewise occurs in Maisch's 'Organic Materia Medica.' This appeared to the writer to be incorrect, and a reference to numerous standard works, both chemical and botanical, as well as actual experiment, has served to confirm its inaccuracy. The well-known test for cellulose, commonly known as "Schweizer's Reagent" (not Schweitzer, as frequently mis-spelled), is an ammoniacal solution of cupric oxide, which has properties quite different from a solution of copper ammonio-sulphate. In Beilstein's 'Handbuch der org. Chemie,' 3rd edt. Bd. i., p. 1,073, with reference to Schweizer, 'Jahresbericht über die Fortschritte der Chemie,'

1857, p. 247, it is simply stated that "Cellulose dissolves in ammonio-cupric oxide (Kupferoxydammoniak)," and that it is precipitated from the solution by acids and *salts*. A similar statement is found in Tollen's 'Handbuch der Kohlenhydrate,' Bd. i., p. 228; Allen's 'Commercial Organic Analysis,' vol. 1, p. 388, and in numerous other works. In Cross and Bevan's work on 'Cellulose,' 1895, p. 13, they note that "Mercer has shown that the reaction of cuprammonium with cellulose is retarded by the presence of salts, and hence that the solutions obtained by decomposing the copper salts with excess of ammonia were much less active than equivalent solutions of the pure hydrate." In Erdmann's 'Lehrbuch der Anorganischen Chemie,' p. 688, reference is made to a basic copper sulphate, obtained by precipitating a solution of the latter salt with such an amount of potassium hydrate that the liquid does not become alkaline, which, when dissolved in ammonia, forms a liquid that is capable of dissolving cellulose. This solution would be quite different, however, from an ordinary solution of copper ammonio-sulphate.

As an experiment, a solution was prepared having twice the strength of the official solution of copper ammonio-sulphate, and pure white cotton was digested with this for a week. At the end of that time the cotton remained quite unchanged, and the liquid, when acidulated, also remained perfectly clear, thus indicating that no cellulose had been dissolved. On the other hand a solution of ammonio-cupric oxide, prepared by precipitating cupric hydrate in the presence of a little ammonium chloride and dissolving the well-washed precipitate in a 20 per cent. solution of ammonia, dissolved cotton abundantly and almost immediately. This solution, when acidulated, afforded the characteristic gelatinous precipitate of cellulose.

It appears that the ammoniacal solution of cupric oxide is occasionally confused with the solution of copper ammonio-sulphate, and this is probably the explanation of the error in the Pharmacopæia. This occurs, for example, in the *Pharm. Journ.*, September, 1899, p. 285, where, in an abstract, it is stated that "for the volumetric determination of alkaloids E. Falieres advocates the use of an *ammoniacal solution of cupric oxide*," and immediately following, that "the copper solution is prepared by dissolving cupric sulphate in water, adding ammonia, etc." The two solutions are, of course, not identical, either in their composition or properties.

Creosote.

This is such a complex substance, and also so variable in composition, that the determination of correct standards for its quality or purity is attended with considerable difficulty. There appears, however, to be one error in the text of the Pharmacopœia, namely, the statement that "it rotates the plane of a ray of polarised light to the left." In the Pharmacopœia of 1885 it was stated to rotate polarised light to the right. J. C. Umney (*Pharm. Journ.*, January, 1900, p. 8), in commenting on this subject, remarks that "as a matter of fact practically all the beechwood creosote found in commerce is either slightly dextro-rotatory or devoid of optical rotation." Allen, 'Commercial Organic Analysis,' vol. ii., part 2. p. 285, makes the following comment:—"Creosote is commonly stated to be optically active. The British Pharmacopœia of 1885 alleged that it was dextro-rotatory, while the edition of 1898 asserts that it is lævo-rotatory, both statements being misleading. As a rule, wood-creosote exhibits no sensible optical activity." Five different specimens examined by the writer, and more fully described below, were found to be *perfectly inactive optically*. An error occurs in Allen's work, *loc. cit.*, p. 277, in the statement that "wood-creosote does not coagulate albumin."

It was thought of interest to ascertain the characters of some commercial creosotes, and the following specimens were therefore procured, and their physical constants determined. They were designated as follows :—

(1) Beechwood creosote, first quality.
(2) Beechwood creosote, second quality.
(3) Wood-tar creosote, first quality
(4) Wood-tar creosote, second quality.

All of the above were obtained from an English manufacturer.

(5) Pure beechwood creosote.

The latter was an old specimen of French origin.

	(1)	(2)	(3)	(4)	(5)
Specific gravity at 15° C.....	1·089 ...	1·089 ...	1·079 ...	1·058 ...	1·085
Polarisation.....	All optically inactive.				
Diminution of volume when shaken with 5 volumes of 10 p.c. NH_3.....	15 p.c....	13 p.c....	5 p.c. ..	2·5 p.c....	4 p.c.

On distilling 100 C.c. the following results were obtained, the mercury being entirely in the vapour of the liquid :—

(1)	190-200° C. (7 p.c.) ;	200-220° (84·4 p.c.) ;	220-240° (8.p.c.)
(2)	—	210-220° (27 p.c.) ;	220-240° (66 p.c.) ; 240-260° (5 p.c.)
(3)	—	210-220° (23 p.c.) ;	220-233° (75 p.c.)
(4)	—	—	230-240° (49 p.c.) ; 240-260° (50 p.c.)
(5)	190-200° (2 p.c.) ;	200-220° (86 p.c.) ;	220-233° (10 p.c.)

The specific gravity may apparently be safely required to be not below 1·080 at 15° C. The present U.S., German, and Swiss Pharmacopœias state not below 1·070, and the French Codex 1·067. Other characters might be more correctly expressed if required to be *optically inactive, or nearly so*, and that it should distil, *for the most part*, between 200° and 220° C. The test with 10 per cent. ammonia does not appear to be of special value, inasmuch as the purest creosote shows the greatest diminution of volume.

The U.S., German, and Swiss Pharmacopœias include a test for propyl-guaiacol (cœrulignol) and other objectionable impurities by shaking creosote with twice its volume of petroleum spirit and baryta water. This test is evidently of some importance. In the specimens examined (2) gave a blue colour in the petroleum spirit layer, and with (4) the aqueous layer was coloured a deep red ; the other samples gave no very marked reaction.

Iron Arsenate.

This salt is, fortunately, recognised by but few modern pharmacopœias. Even those which have adopted it give different methods for its preparation, and, as found in commerce, it appears to be quite variable in composition. The official method of preparation and determination has already been criticised to some extent by Thos. S. Barrie (*Chemist and Druggist*, May, 1900, p. 884). With regard to the proportions given in the process for its preparation, Mr. Barrie notes that "the amount of sodium arsenate is excessive, and that 20½ ounces is sufficient for the complete precipitation of the iron." If one takes the pains to examine the subject a little more closely, it will indeed be found full of perplexity. The Pharmacopœia directs crystallised ferrous sulphate and anhydrous sodium arsenate to be used, and, it we assume the reaction to take place according to the following essential factors of the equation, it may be represented as follows :—

$$3FeSO_4 \cdot 7H_2O + 2Na_2HAsO_4 = Fe_3(AsO_4)_2$$

$$834 \cdot 6 \qquad 372 \cdot 22$$

Thus 415 grammes of ferrous sulphate would require, theoretically, 185 grammes of sodium arsenate, instead of 530 grammes, or 20¾ oz. of ferrous sulphate would require 9¼ oz. of sodium arsenate, instead of 26½ oz., as prescribed. The 1885 Pharmacopœia directed for the same amount of ferrous sulphate 15¾ oz. of anhydrous sodium arsenate, an amount still largely in excess. Even if the amount of sodium arsenate were calculated for the crystallised salt it would still be considerably in excess, for the above amount of ferrous sulphate would then require 310·5 grammes and 15½ oz. of sodium arsenate respectively.

The process given in the French Codex appears still more inconsistent, since the latter directs for 10 parts of ferrous sulphate 50 parts of crystallised sodium arsenate, corresponding to 29·8 parts of the anhydrous salt. This would be equivalent to 1236·7 grammes of anhydrous sodium arsenate for 415 grammes of crystallised ferrous sulphate. The French Codex, however, assigns to the salt the composition $FeHAsO_4$, and therefore directs no sodium bicarbonate to be used in its preparation. It must thus be considered that the Codex assumes the reaction to take place as follows :—

$$\underset{278\cdot2}{FeSO_4\cdot7H_2O} + \underset{312\cdot25}{Na_2HAsO_4\cdot7H_2O} = FeHAsO_4 + Na_2SO_4 + 14H_2O.$$

These proportions would correspond theoretically to 11·22 parts of crystallised sodium arsenate for 10 parts of ferrous sulphate, and the proportion directed of the former therefore appears to be enormously in excess. It is, moreover, not at all probable that a salt of the composition indicated is formed by this reaction. (Compare also the criticisms by Hirsch, ' Universal Pharmakopöe,' Bd. i., p. 672).

Mr. Barrie (*loc. cit.*) has further criticised the Pharmacopœia requirement that only the ferrous iron in this salt shall be determined. With consideration of the potency of this preparation, together with the fact that only one qualitative test for purity is given—namely, that for *sulphates*, it also appears to the writer that the determination of the arsenic acid is of infinitely more importance.

Saccharated Iron Carbonate.

The definition of the chemical character of this preparation, as given by the Pharmacopœia, does not seem sufficiently precise to be of much utility, and might just as well be omitted. Thus " x $FeCO_3$ and y $Fe(OH)_2$, more or less oxidised," would also imply z Fe_2O_3. It, moreover, does not seem quite correct or logical to speak of a " ferrous oxycarbonate, more or less oxidised," and it is also doubtful whether a mixture dried at 100° C. would contain any ferrous hydroxide $Fe(OH)_2$.

Iron and Quinine Citrate.

The estimation of the quinine in this salt is much more conveniently accomplished with the use of chloroform than of ether.

Exsiccated Ferrous Sulphate.

The text of this preparation would appear to admit of some improvement. Instead of directing that ferrous sulphate should be exposed to heat " until aqueous vapour ceases to be given off," and that " the residue should weigh *about* 60 per cent. of the original salt," it would seem much more practical and convenient to prescribe a definite loss of weight, which in the United States, German and Swiss Pharmacopœias is uniformly fixed at 35-36 per cent. The quantitative test also appears to be very awkwardly expressed, inasmuch as it requires the product to contain an amount of iron corresponding to at least 92½ per cent. of $FeSO_4\cdot H_2O$. As the product does not correspond exactly to a salt of the latter formula, there is no apparent advantage in basing the calculation upon it. If a quantitative test is considered necessary, it would be much more simply expressed by requiring a certain percentage of iron in the ferrous state.

Reduced Iron.

The official method or determining the amount of metallic iron in this preparation is not a satisfactory one, and the details are not quite correctly expressed. A more accurate method is that with the use of mercuric chloride and potassium iodide, as formulated either by the United States or German Pharmacopœias (compare E. Merck, the *Chemist and Druggist*, Aug., 1898, p. 348, also E. S. Peck, in the *Pharm. Journ.*, Aug., 1898, p. 159, and July 1899, p. 109). A test for *arsenic* would also be desirable.

Tartarated Iron.

The Pharmacopœia prescribes the following method for determining the iron in this salt. "By incinerating 10 grammes at a red heat, washing the residue in water, and again incinerating with free access of air, a residue of ferric oxide is obtained weighing not less than 3 grammes." Although this may seem a very simple operation, anyone who has conducted it will appreciate the difficulty of washing out the potassium carbonate from the resulting light carbonaceous mass or of completely burning away the carbon, and even with the greatest care in these manipulations it is almost impossible to avoid loss and obtain approximately accurate results. It is therefore quite inexplicable why this method should be adopted in preference to the iodometric one, which is so much more simple, expeditious, and accurate, and which, as formulated by the United States and German Pharmacopœias, is applicable for the determination of iron in all the so-called scale salts, as also in the official solutions of iron. It was thought of interest to determine the percentage of iron in tartarated iron and also in the iron and ammonium citrate by the iodometric method, and to compare these results with the official requirements by the method of ignition. For this purpose a sample of each of these salts was obtained from three of the leading London manufacturers, which may be designated respectively as A, B, and C. The iodometric estimations were conducted as described in the United States Pharmacopœia. Two determinations were made of each salt, and the mean of the closely agreeing results taken.

Tartarated Iron.

(*a*) Contained 19.95 per cent. Fe = 28.50 per cent. Fe_2O_3.
(*b*) ,, 18.93 per cent. Fe = 27.04 per cent. Fe_2O_3.
(*c*) ,, 17.10 per cent. Fe = 24.43 per cent. Fe_2O_3.

The Pharmacopœia requires the salt to yield, by the method of ignition, not less than 30 per cent. of ferric oxide.

Iron and Ammonium Citrate.

	By Iodometric Method.	By Ignition.
(*a*) Contained	20.76 p. c. Fe = 29.66 p. c. Fe_2O_3	. . 30.75 p. c. Fe_2O_3.
(*b*) ,,	20.42 p. c. Fe = 29.17 p. c. Fe_2O_3	. . 32.56 p. c. Fe_2O_3.
(*c*) ,,	20.80 p. c. Fe = 29.70 p. c. Fe_2O_3	. . 31.86 p. c. Fe_2O_3.

The Pharmacopœia requires this salt to yield, by the method of ignition, 31 or 32 per cent. of ferric oxide, and the three specimens may be considered to meet this requirement; but at the same time, the iodometric method, which gives somewhat lower results, undoubtedly indicates more correctly the actual percentages of iron contained in the salts. The difference in the results may be partly attributed to the presence of alkali, for the residues of ferric oxide from all the samples of this salt were alkaline to litmus, and the salt B, which afforded the highest percentage of ferric oxide, was also the most strongly alkaline.

Hyoscine Hydrobromide and Hyoscamine Sulphate

Compare notes under Atropine.

Lithium Carbonate.

Some notes of interest relating to the characters and examination of this salt are given by L. F. Kebler (*Amer. Journ. Pharm.*, 1898, p. 600, *Pharm. Journ.*, December, 1898, p. 689).

Lithium Citrate.

From the figures given in the text for this salt it is assumed that when dried at 100° C. it loses 3 molecules of water, and at 115.5° C. an additional molecule, the salt thus dried being then required to yield on ignition a residue corresponding to 98.5 per cent. of the pure citrate. These requirements, although precisely stated, are not quite correct, and in practice cannot be met. In the first place, there is no indication of the length of time at which the salt should be dried at the specified temperatures, and at 100° C. a constant weight cannot be obtained. In the second place all the water is not expelled at 115.5° C. (a statement also occuring in the French Codex), and a temperature of about 140° C. seems to be necessary. A more satisfactory method of determining the percentage of pure lithium citrate in the salt is by its conversion into sulphate (compare L. F. Kebler, *Amer. Journ. Pharm.*, 1899, p. 137, also E. Merck, *Chemist and Druggist*, August, 1898, p. 348).

The French Codex contains some peculiar errors in the text for this salt, as, for example, the statement (originating with Dorvault) that it is soluble in 25 parts of water. It also states that 1 gramme of the salt, when calcined with an excess of sulphuric acid, leaves 0.225 gramme of lithium sulphate, whereas the calculated amount of the latter is 0.585 gramme.

Magnesium Carbonate.

The same criticism would apply to the formula for this salt as to those given for bismuth subcarbonate and bismuth subnitrate. It is well known that the salt is of somewhat variable composition, and therefore cannot be represented by a definite formula such as that assigned to it by the Pharmacopœia, which nearly corresponds with that of the French Codex.

Menthol.

Messrs. Schimmel and Co. (*Semi-Annual Report*, October, 1898, p. 63) have commented on the Pharmacopœia description of this substance as being "in crystals usually more or less moist from adhering oil," and have noted that recognition is thus given to an impure article.

The colour reaction stated to be obtained when menthol is "boiled with sulphuric acid diluted with half its volume of water" is of exceedingly doubtful value.

Morphine Hydrochloride.

This salt is described as forming "acicular prisms, or a white powder consisting of *minute cubical crystals*." A similar description is given in the United States and Swiss Pharmacopœias, but it appears very doubtful whether the white powder form of the salt consists of minute *cubical* crystals. The German Pharmacopœia describes it as occurring in "white needle-shaped crystals, or white cubical pieces (Stücke) of a micro-crystalline character." Beilstein ('Handbuch,' Bd. iii., p. 898), referring to Hesse, states that by slow crystallisation from alcohol the *anhydrous* salt is obtained in the form of short, four-sided rhombic prisms, and Guareschi ('Die Alkaloide,' p. 371) gives a similar description, together with that of the German Pharmacopœia. The salt would evidently be more correctly described as "in acicular crystals, or a white micro-crystalline powder." It is possible that an explanation of the apparent error may be found in the fact that for some time past certain manufacturers have brought morphine salts into commerce in the form of small, artificially-formed cubes, but the crystals of which

these are composed are not cubical. Compare also E. Merck (*Chemist and Druggist*, August, 1898, p. 348).

Expressed Oil of Almond.

J. C. Umney (*Pharm. Journ.*, July, 1899, p. 106, and January, 1900, p. 8) considers the test with fuming nitric acid to be incapable of detecting the presence of peach kernel oil, but useful for detecting apricot kernel oil. The U.S. Pharmacopœia (1890) has adopted this test for the detection of peach kernel oil, and the Swiss Pharmacopœia gives it as a specific test for the latter *(Pfirsichkernöl)*, as also for rape-seed oil *(Repsöl)*. Mr. Umney's observations are of special interest, as the tests were made with pure oils of peach kernels and apricot kernels, obtained both by expression and by extraction with ether. There is, however, an explanation which may serve to clear up this apparent discrepancy. According to Hirsch ('Commentar zum Arzneibuch für das Deutsche Reich,' p. 483), under the name of "Pfirsichkernen" (the only English equivalent for which is peach kernels), which are used in making the so called *oleum amygdalarum gallicum*, are not to be understood the kernels of the common peach (*Prunus Persica*, Jess, *Amygdalus Persica*, Linné, or *Persica Vulgaris*, Mill), but a small sort of the bitter almond, a variety of *Amygdalus communis*, Linné. This oil undoubtedly affords the reaction described in the Pharmacopœias.

Oil of Cloves.

A useful criterion for the purity of this oil, which might be considered by the Pharmacopœia, is its property of forming a clear solution with twice its volume of 70 per cent. alcohol.

Oil of Cinnamon.

For determining the percentage of cinnamic aldehyde, or of non-aldehyde constituents, in this oil, the Pharmacopœia directs that "if 10 C.c. be *well shaken with* 50 *C.c. of a boiling* 30 *per cent. solution of sodium hydrogen sulphite*, an oily layer separates, which, when cooled to 60° F., should not measure more than 5 C.c." These directions are quite inadequate, and in many cases would lead to very incorrect results, if not to complete failure. In the first place, it would obviously be a very difficult matter to shake the oil with a *boiling* solution of sodium hydrogen sulphite, and it is furthermore not desirable to add the entire amount of the latter solution at once, but in small portions, the flask being heated on a water-bath after each successive addition of the solution until the solid bisulphite compound has become completely liquefied. A proper description of the method of conducting this determination is given by Gildemeister and Hoffmann in 'Die aetherischen Oele,' Berlin, 1899, p. 505. A test for the purity of this oil, which is also of some value, is its property of forming a clear solution with three times its volume of 70 per cent. alcohol.

Oil of Copaiba.

In the *Pharm. Journ.*, January, 1900, p. 54, F. W. Short criticises the statement of the Pharmacopœia that this oil "should rotate a ray of polarised light from 28° to 34° to the left." This statement occurs under Copaiba, but in the text of the oil the factors of rotation are not mentioned. As Mr. Short has pointed out, they are misleading, for the limits of rotation should be much broader. A specific test for *gurjun oil* might be adopted (see *Amer. Journ. Pharm.*, 1897, p. 579), although this would also be indicated by a higher specific gravity and a higher optical rotation.

Castor Oil.

The Pharmacopœia has adopted a test with sulphuric acid or the detection of foreign oils, which is essentially the same as that given in the United States and

German Pharmacopœias, but by introducing the slight verbal change of requiring that "the mixture should not become *brown*, instead of *blackish-brown*, the character of the test has been rendered inaccurate. (See also *Pharmaceutical Journal*, January, 1900, p. 8.)

Some brief critical notes on several of the official oils have also been communicated by E. Dowzard, to which reference may be made (*Chemist and Druggist*, May, 1899, p. 814).

Physostigmine Sulphate.

This salt might, with advantage, be replaced by the salicylate, which is much more stable, and therefore more largely used. The Pharmacopœia indicates the sulphate to contain an indefinite amount of water of crystallisation, expressed as "xH_2O," but it is probable that, like the salicylate, the salt is really anhydrous, and that any water it may contain is simply hygroscopic moisture, due to its deliquescent character. Guareschi ('Die Alkaloide,' p. 495) regards it as anhydrous.

Pilocarpine Nitrate.

The Pharmacopœia has wisely adopted this salt of pilocarpine in preference to the hydrochloride, which is somewhat deliquescent. The text, however, is very imperfect (compare papers on this subject by Dr. H. A. D. Jowett, *Pharm. Journ.*, July, 1899, p. 91, and *Journ. Chem. Soc.*, 1900, p. 473). Subsequent observations would suggest a slight modification of two of the factors given for this salt in the first-mentioned paper, in order that they may meet practical requirements. The melting point should be not below 173° C., and the specific rotation not lower than + 80°. The formation of a crystalline picrate, which melts quite sharply at 147° C., is also a useful criterion for the purity of this salt.

Potassium Tartrate.

The formula given in the Pharmacopœia for this salt is incorrect. It should be $(K_2C_4H_4O_6)_2 \cdot H_2O$, and the official requirement of the volumetric test is based upon the latter formula. If the salt had the formula $K_2C_4H_4O_6 \cdot H_2O$ one gramme of it, after ignition, would require about 8·2 C.c. of normal sulphuric acid for neutralisation, instead of 8·4 C.c., or, more correctly, 8·5 C.c. The error has probably arisen through the attempt to express the composition of the salt by a constitutional formula (see also *Pharm. Journ.*, September, 1899, p. 284).

Acid Quinine Hydrochloride.

E. Merck (*Chemist and Druggist*, August, 1898, p. 349) has noted that it is practically impossible to titrate this salt with normal alkali, the results with litmus as an indicator being too low, and with phenolphthalein, or methyl orange, excessively high.

Quinine Sulphate.

Some interesting observations and criticisms relating to the official test for this salt are noted by A. J. Cownley and by David Howard (*Pharm. Journ.*, vol. lx., 1898, pp. 412, 447, 472).

Sodium Arsenate.

Thos. S. Barrie (*Chemist and Druggist*, May, 1900, p. 884) has justly criticised the official method for the quantitative determination of the purity of this salt by means of lead acetate. It is quite certain that no careful analyst would think of employing this method, and a quantitative determination can hardly be considered of value unless it is reasonably accurate. Moreover the figures given for the test appear to be wrong, for, as Mr. Barrie has noted, 1 gramme of the salt would require 3.05 grammes of lead acetate for precipitation, instead of 2.03 grammes,

the Pharmacopœia having assumed that an acid, and not the neutral lead arsenate, is formed, or there is possibly a typographical error (see also *Pharm. Journ.*, September, 1899, pp. 324, 355).

Sodium Hypophosphite.

See note under calcium hypophosphite.

Solution of Lead Subacetate.

The writer has found that this solution (sp. gr. 1.277), when freshly prepared, requires for 1 gramme 19 C.c. of decinormal sulphuric acid for complete precipitation. The lower figure, 17 C.c., given by the Pharmacopœia, would allow for the change which this solution rapidly undergoes. In the determination of the lead it is an advantage to dilute the solution with water and use methyl orange as an indicator.

Sulphur.

It is somewhat surprising that the Pharmacopœia should make the requirement that sublimed sulphur "should not have any action upon litmus," and that "solution of ammonia, agitated with it, and filtered, does not on evaporation leave any residue." It is quite well known, as has been noted by E. Merck (*Chemist and Druggist*, August, 1898, p. 349), that neither of these requirements can be met. For this reason most of the modern Pharmacopœias have adopted as a special preparation for medicinal use a purified sulphur, *sulphur lotum*, U.S. and Swiss; *sulfur depuratum*, Germ.; or *soufre sublimé lavé*, French Codex, from which the free acid and arsenious sulphide or arsenious acid have been removed by digesting sublimed sulphur with dilute ammonia and washing with water.

Terebene.

Besides the British, this preparation is only recognised by the United States and Russian Pharmacopœias. Although of complex composition, and therefore somewhat variable in character, it admits of somewhat more precise and accurate description than is given by the Pharmacopœia. A chemical study of its constituents was made a few years ago by Power and Kleber (*Pharm. Rundschau*, New York, 1894, pp. 16-19), and from the results of that investigation it was proposed that it should be defined as "consisting for the most part of the hydrocarbons dipentene and terpinene, with some cymol and camphene." The preparation employed in that research represented a product that had been carefully prepared on a large scale. It was optically inactive, had a specific gravity of 0.855 at 15° C., and distilled chiefly between 170 and 185° C.

Three specimens of terebene have recently been obtained from leading London manufacturers and examined, with the following result. The samples may be designated as A, B, and C:—

	A	B	C
Specific gravity at 15° C.	0.863	0.862	0.865
Optical rotation in 100 Mm. tube	—0.15′	—0.30′	Inactive.
Fractional distillation of 100 C.c.	—	—	—
—165° C.	1.0 C.c.	— C.c.	1.5 C.c.
165—170° C.	4.0 ,,	1.6 ,,	15.5 ,,
170—175° C.	24.4 ,,	38.0 ,,	44.5 ,,
175—180° C.	38.0 ,,	33.2 ,,	24.0 ,,
180—190° C.	27.0 ,,	21.2 ,,	8.5 ,,
Residue	5.6 ,,	6.0 ,,	6.0 ,,
	100.0	100.0	100.0

It will be observed that the specific gravities of all the samples are in close accordance with the official requirements. The lower specific gravity referred to (0.855), as observed by the writer, may be attributable to the use of a more freshly

distilled oil of turpentine, although the specific gravity of terebene itself will also become increased by age. The statements of the Pharmacopœia that "it should distil between 156° and 180° C.," and that "not more than 15 per cent. should distil below 165° C." obviously require modification. It could not distil at the lower temperature unless it contained unaltered pinene, which would not be the case in a carefully prepared article, and which would also be indicated by its optical activity. It might properly be required to distil chiefly between 170° and 185°, or possibly 190° C. To permit as much as 15 per cent. to distil below 165° C. would admit a very inferior preparation. It has been noted by several manufacturers ('Year Book of Pharmacy,' 1899, p. 396, and *Pharm. Journ.*, July, 1899, p. 104, January, 1900, p. 8) that a terebene made from American oil of turpentine may be slightly lævorotatory, as is indeed the case in two of the specimens examined, or that when originally inactive it may acquire optical activity on keeping. In this connection the observation of Dr. J. H. Long (*Journ. Amer. Chem. Soc.*, 1894, p. 844) is of interest, that American oil of turpentine sometimes has a very low positive rotation, or may even be lævorotatory, when containing the product distilled from the so-called spruce trees. The very slight lævogyrate rotation occasionally observed in terebene may be due to this fact, or possibly to the presence of a little lævogyrate limonene.

Veratrine.

The retention by the Pharmacopœia of a detailed process for the preparation of this alkaloid or mixture of alkaloids when processes for all the other organic principles of this class have been deleted has attracted the attention of several commentators. It would be interesting to know why an official process has been considered necessary for this substance, which is apparently one of the last things that a pharmacist would undertake to manufacture.

Conclusion.

In the preceding observations the writer has not attempted to consider the text of all the chemicals of the Pharmacopœia, but has necessarily restricted his comments to such statements as have from time to time been more prominently brought to his notice by a perusal of the work. Such an inspection, however, appears to indicate that the errors are somewhat more numerous than one might reasonably expect in a work of a national and authoritative character, and it is evident that some of these errors might have been avoided, either by reference to standard chemical works, to current chemical literature, or by simple experiments.

There are naturally also some features of every Pharmacopœia of a more general character, which, quite apart from any actual inaccuracies, may properly form the subject of individual comment, such as its scope or limitations, the arrangement of the text, character of the tests, etc., and a brief reference may be made to some of these.

(1) In the first place, as the Pharmacopœia has wisely omitted details of processes for nearly all the chemicals, which are now made almost exclusively and much more economically on a large scale, it might with advantage have gone a step further, and, in conformity with most of the modern Pharmacopœias, have omitted such information as it gives with respect to the methods by which the official chemicals are obtained. It does not seem probable that from any point of view the very brief and often imperfect information given can serve any useful purpose, as it may be found either in text-books on chemistry or in greater detail in works on chemical technology, to which those who desire to make any practical use of such knowledge will naturally refer. If a few examples be taken at random from the long list one may consider the official description of the methods for

obtaining lead iodide, mercuric iodide, or sodium arsenate, which is totally inadequate for any practical purpose, for it is quite important in the preparation of these chemicals, as indeed in most others, that definite proportions of the combining substances be employed, independent of motives of economy. In the case of sodium sulphocarbolate it is stated that "it may be obtained *by dissolving phenol in excess of sulphuric acid*, and converting the phenol-sulphonic acid so obtained into a sodium salt." The required para phenolsulphonic acid may *not* be obtained by simply dissolving phenol in sulphuric acid, and, besides, what is to be understood by an *excess* of the latter, and how is it to be removed? The statement under the corresponding zinc salt is more nearly correct, as it is said "it may be obtained *by heating a mixture of phenol and sulphuric acid*, etc.," the word "excess" being omitted, and *heating* being specified, but here also the temperature at which the mixture is heated is of some importance. The formula of the zinc salt is wrong, as it contains 8 molecules of water. The information given regarding the production of sulphur, sodium carbonate and bicarbonate, mercuric and mercurous chloride, potassium nitrate, and innumerable other salts can hardly be considered necessary for the pharmacist or of particular value to any of those who require to make use of the Pharmacopœia, who may be assumed to possess a knowledge of these elementary facts. From an explanation given in the Preface, however, it would appear that this feature of the work is obligatory, since it contains (page xiii.) the following statement:—"The paragraphs in former editions which were more or less descriptive of the sources or modes of preparation of official chemical substances have been abbreviated *as far as the requirements of the Medical Act of* 1858 *will permit*."

(2) There does not seem to be perfect uniformity in expressing the formulas of the official chemicals, as may be observed, for example, in the formulas for tartarated antimony and sodium potassium tartrate or potassium acetate and lead acetate. Among the reagents methyl orange and phenol-phthalein, which are only used as indicators, are given constitutional formulas, or, in the case of the last named, a complete structural formula. In the Preface (page xiv.) it is stated that "extended structural or graphic formulæ, which would often occupy the space of several lines of print, have, as a rule, been excluded," but it is not quite clear why it should have been considered necessary in this single instance. For all the purposes of a Pharmacopœia the simplest empirical formulas would doubtless be quite sufficient, but in connection with these it would be useful to state the respective molecular weights.

(3) In the text of the various chemicals we meet with such statements as the following one under lithium citrate:—"It yields the reactions characteristic of lithium and of citrates," or under lead oxide:—"It gives the reactions of lead." Facts of this character would be so self-evident to anyone that it hardly seems necessary to note them unless special tests for identity are given. Throughout the work the expression "characteristic reaction" occurs, as under lead oxide:—"It should yield no *characteristic* reaction with the tests for copper, iron, or carbonates." The word "characteristic" would appear to be superfluous, for it would certainly be understood that a reaction employed in testing for these substances would be one characteristic of them.

(4) The plan adopted for stating the tests for purity, or, rather, the substances to be tested for, may appear to possess the merit of simplicity, but it is a question whether it will not fail in its purpose and tend rather to discourage the testing of chemicals by those who are not, through more or less constant practice, kept conversant with analytical methods. Some of the lists of tests would require the substance to be taken pretty well through the ordinary analytical chart, involving the separation of several groups of elements and several hours' work, and even

then it is likely that some impurity might be overlooked if no special instructions are given. A good example of this is afforded by the text for bismuth carbonate, where it is stated :—" These bismuth salts, *when suitably treated*, should yield no characteristic reaction with the tests for silver, lead, copper, arsenium, iron, zinc, calcium, magnesium, chlorides, or sulphates, nor with the tests for selenium and tellurium." It may be safely asserted that a tolerably good analyst would require to give conserable thought to such a problem before deciding upon tests which would positively confirm the absence of all the above-mentioned elements, without involving their actual separation from each other. The facility with which these tests may be conducted depends very largely in this case upon the simple, but somewhat ambiguous, phrase—" when suitably treated."

Another example is afforded by the text of cerium oxalate, where it is stated that it should yield no characteristic reaction for various substances, including *calcium*. On refering to the lists of tests given in the Appendix, there will be found under calcium two positive tests—namely, that " solution of ammonium carbonate yields a white precipitate, etc.," and that " solution of ammonium oxalate gives a white precipitate, etc.," also as a negative test that " solution of potassium chromate gives no precipitate," but none of these tests are applicable for the direct detection of calcium in cerium oxalate.

An apparent justification of the plan adopted by the Pharmacopœia with respect to the omission of specific tests for the detection of impurities in chemicals is afforded by the following explanatory statement in the Preface (page xiv.):— " Nor are manipulative details set forth at length, either as regards the preparation of a substance for testing, or as regards the solution or application of the tests, *the pharmacist being assumed to possess full knowledge of these and all similar points.*" If it be assumed that the pharmacist possesses such full knowledge on these important points, it certainly does not seem quite consistent that it should be considered necessary to explain how all the chemical preparations of the Pharmacopœia are obtained.

(5) In some cases, however, specific tests are given in the Pharmacopœia, as, for example, the test for thiocyanates in potassium bromide. The necessity for such exceptions to the general rule is not obvious, for anyone capable of conducting the tests for the other substances mentioned—lead, copper, arsenium, iron, aluminium, zinc, calcium, magnesium, sodium, ammonium, bromates, iodates, cyanides, etc. —will in all probability also be familiar with the simple test for thiocyanates, or could at least refer to it in some chemical work.

Under potassium carbonate it is stated that " it should yield *only the slightest reactions* with the tests for iron," and *no strongly-marked reactions* with the tests for chlorides." It is difficult to surmise what difference in the intensity of the reactions is intended to be permitted in these two differently-worded tests. Neither form of expression is sufficiently precise, for no definite standard of purity can be maintained or required when it is left entirely to individual judgment to decide as to what may constitute a strongly-marked or slight reaction. In some cases the Pharmacopœia appears to have gone to the opposite extreme in being unduly exacting in its requirements, as, for example, under sodium, where it is stated that "*each* gramme very cautiously added to water affords a solution which should require for neutralisation at least 42·6 C.c. of the volumetric solution of sulphuric acid." The purity of commercial metallic sodium is such that there would seem to be no practical necessity for a quantitative test of this character.

(6) The question may be suggested whether it would not be an advantage to those using the Pharmacopœia if the impurities to be tested for were rendered more prominent by placing them in italics, rather than the names of the reagents used for their detection, or as tests for identity.

(7) "*Articles Employed in Chemical Testing.*"—In this list a method is given for preparing barium hydroxide, which appears quite unnecessary, since it is as easily available an article of commerce as the Barium Chloride which precedes it. One reagent occurs twice in the list, as "*calcium oxide*—the lime of the British Pharmacopœia," and as "*lime*—the lime of the British Pharmacopœia." Considerable space might be saved by the omission of the frequently-repeated words, "of the British Pharmacopœia," and the desired purpose would be just as well accomplished if a simple statement were made at the head of the chapter that such articles as are employed in chemical testing, when represented in the Pharmacopœia, or unless otherwise indicated, should respond to its tests for purity. Even under water the specific requirement is made that it shall be "the distilled water of the British Pharmacopœia." The requirement that the test-solution of ferric chloride should be made from anhydrous ferric chloride has been commented on under Acetanilide. *Nessler's reagent* has been brought as a synonym under the title "solution of potassio-mercuric iodide," and is referred to under that title in the tests for distilled water. The latter designation, however, is commonly understood to apply to the so-called *Mayer's reagent*. The more correct title of the official solution would be alkaline solution of potassio-mercuric iodide.

Under the reagent sodium thiosulphate, p. 402, it is required that "2,4644 grammes should decolorise 100 *cubic centimetres* of the volumetric solution of iodine." The use of this amount of substance would involve a quite unnecessary waste of iodine solution, as equally accurate results may be obtained with one-fourth the quantities specified. It is in marked contrast to the requirement for example, under sodium potassium tartrate, that "each gramme, heated, etc., should require for exact neutralisation at least 7 C.c. of the volumetric solution of sulphuric acid." In the Preface, however, there is also a paragraph (pp. 14, 15) which may be considered to explain, although not altogether satisfactorily, this apparent lack of consistency, since it states: "In quantitative testing the specified amounts of solid or liquid substances are intended only as proportions indicating official standards of purity." . . . . "In short, the procedure in these and other chemical operations is now left to the skill and judgment of workers *who are assumed to be duly trained.*" In this case it would be much simpler to indicate only the percentage of purity required, without any details whatever, but if quantities such as 2,4644 grammes and 100 C.c. are specified, there is no reason why they should not represent such as may be more conveniently and more judiciously employed.

In concluding these somewhat extended observations, the writer desires to express his thanks to Mr. Frank Shedden, B.Sc., A.I.C., of the laboratory staff, who has assisted him in some of the experimental work connected therewith, and at the same time to entertain the hope that some at least of the recorded notes and comments may prove useful to those upon whom the preparation of a subsequent edition of the British Pharmacopœia may devolve.

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