COMMENT ON THE U. S. P. X WITH REFERENCE TO THE FORTHCOMING REVISION.*

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The actual use of the Pharmacopœia after the new revision appears always brings to mind certain conditions which appear to require attention in the next revision. There usually are certain questions of policy on which comments can be made. Various tests appear to require some correction in the light of practical experience and application. Now and then wording seems ambiguous and needs to be changed. Pharmaceutical, medical and biological research results in the perfection of new and important products which acquire wide use and therefore should be considered as additions. Certain definitions do not appear to be as definite as they might be. Changes in certain formulas appear advisable and added tests and standards suggest themselves. As the Pharmacopœial Convention will meet in Washington[1] next week to determine upon general principles to be followed in the forthcoming revision, elect a Revision Committee and authorize this committee to proceed with its work, it is appropriate that such suggestions as we may have accumulated in our respective use of the Pharmacopœia should be presented at this time so that they will come to the attention of those interested, and this paper is written to serve this particular purpose without attempting to go into great detail in connection with the individual recommendations. I have classified the items under various headings, as a matter of convenience.

(*1*) *Pharmacopœial Policy.*

Definition of the words "antiseptic" and "germicide." It would seem advisable to have the Pharmacopœia consider furnishing official definitions for the meaning of the words "antiseptic" and "germicide" together with appropriate tests to determine to what extent preparations sold for one or the other purpose have these properties and set a standard below which the products claimed to be antiseptic or germicidal should not fall.

Regular Supplements. It is believed desirable to have supplements to the Pharmacopœia issued at regular intervals. This subject is discussed in further detail in another paper.

(*2*) *Recommendations for Additions to U. S. P.*

The following preparations appear to have sufficiently wide use and have proved their therapeutic merit through such use so that they are well worthy of consideration for recognition in the U. S. P. XI.

Insulin, Ephedrine—alkaloid and salts—Sulpharsphenamine, Ovarian Hormone and Calcium Gluconate.

(*3*) *Added Tests and Standards.*

It would appear desirable for the U. S. P. XI to add a standard on vitamin D for Cod Liver Oil. Satisfactory biological assay methods for determination of vitamin D have been perfected in several laboratories and published.

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* Section on Practical Pharmacy and Dispensing, A. PH. A., Baltimore meeting, 1930.

[1] Has convened.

It would appear desirable to establish a standard for glycyrrhizin content for licorice and its preparations and furnish suitable assay method for this purpose.

The U. S. P. X gives the alcohol content range of most alcoholic preparations. However, the general method for determining alcohol content is not applicable to all preparations. It would appear advisable to give information as to how alcohol content should be determined for the several classes of preparations and special directions or precautions for those products in which the general methods will need changes.

An assay method for mercuric oxide should be given for Yellow Oxide of Mercury Ointment. Our and other laboratories have published papers on suitable assay processes.

(4) *Formula Changes.*

Tincture of Aconite U. S. P. is quite unstable. Adjustment of the p_H of the preparation to a definite point by use of a suitable amount of acid in the menstruum greatly improves the stability and it is highly desirable that a suitable change in formula to effect proper p_H of the finished product be made. Several papers giving detailed information have been published from our and other laboratories.

Ointment of Zinc Oxide seems to be entirely too stiff to be satisfactory for general use and it would seem desirable to change the paraffin content from 15 to about 5%.

Ointment of Boric Acid U. S. P. X has caused a good deal of complaint because of its color. I am not sure that even to-day the public or the professions are reconciled to the present official ointment. It may be wise to consider utilizing white wax or paraffin and white petrolatum instead of yellow wax and yellow petrolatum as a base. If the yellow ointment has been accepted it will no doubt be best to stay with it as further change would again cause confusion. The ointment of the U. S. P. IX was white and the change made in the U. S. P. X seemed a minor one from a therapeutic standpoint and proved very unpopular generally, which indicates the inadvisability of striking changes in Pharmacopœial preparations except for important reasons.

Sulphur Ointment. Benzoinated lard prescribed as a vehicle for this ointment does not make a particularly satisfactory preparation, is subject to rancidity and granulation in warm weather. It would seem that the substitution of a mixture of lanolin and white petrolatum would make a more stable and satisfactory ointment without damaging its therapeutic properties.

Fluidextract of Squill is directed to be made with diluted alcohol, and it is almost impossible to percolate squill with a menstruum of this alcoholic strength because of absorption of water by the squill from the menstruum with consequent swelling and gelatinization. A menstruum of a strong alcoholic content is much more satisfactory and appears to extract the active principles equally well.

(5) *Corrections in U. S. P. Tests.*

Arsenic Test for Bismuth Salts. The Pharmacopœia directs that Bettendorf's test be used and the general impression is that the Gutzeit test cannot be used for bismuth preparations. We have found, however, that the Gutzeit test can be used satisfactorily on bismuth salts and as it is more accurate it seems preferable.

Arsenic Test for Barium Sulphate. It has been found that the Gutzeit test is entirely satisfactory for determining arsenic and barium sulphate. In view of its greater accuracy it would appear a more desirable test.

Castor Oil. The U. S. P. X states that castor oil is only partly soluble in petroleum benzin but yields a clear liquid with an equal volume of alcohol. We have found that castor oil sometimes yields clear mixtures with certain proportions of petroleum benzin. We attribute this not so much to differences in castor oil as to differences in petroleum benzin. The reference to its solubility probably should be eliminated or petroleum benzin of very definite specifications called for.

Whisky. Under tests for identity and purity there is given one intended to show whether or not isopropyl alcohol is present. This test will not detect the presence of pure isopropyl alcohol but only such commercial varieties as are contaminated with tertiary butyl alcohol and is in fact a test for tertiary butyl alcohol rather than isopropyl alcohol. No doubt an additional test suitable for detecting isopropyl alcohol should be included.

Benzoin. Under test for identity the U. S. P. X states that one Gm. of benzoin extracted with carbon disulphide should yield a residue not exceeding $12^1/_2\%$. Benzoin yields a larger amount of residue and in fact in Siam benzoin this residue will average about 60%. It no doubt was intended that the Pharmacopœia should read "not less than" instead of "does not exceed" $12^1/_2\%$.

Alcohol Determinations. The directions given on pages 427–428 of the U. S. P. X apparently contain a typographical error in that the first sentence of the last paragraph starting on page 427 seems to be misplaced.

Rochelle Salt. According to the U. S. P. this product is alkaline to litmus paper. We generally find this material to be neutral. As the Pharmacopœia also directs that it should not be alkaline to phenolphthalein, it appears that the reference to its reaction to litmus paper is superfluous; but if it is retained it probably should say "neutral or alkaline."

Alum. There is a discrepancy in the figures given in the assay between the factor used and the amount of aluminum oxide corresponding to aluminum ammonium sulphate and aluminum potassium sulphate, respectively.

Dichloramine. The use of an indicator is omitted in the assay, which apparently is an oversight. Starch test solution gives satisfactory results.

Tincture Iron Chloride. In the test for identity there appear in the third line the words "white precipitated," etc., which should be deleted as this is evidently a misplaced fragment of a chloride identity test.

Ammonium Bromide. The solubility of this substance in alcohol as given in the U. S. P. appears incorrect.

Cod Liver Oil. The saponification and iodine value of Cod Liver Oil needs some revision. The present figures are no doubt carried over from the previous U. S. P. which recognized only the oil of cod fish livers, whereas the present Pharmacopœia recognizes oils obtained from livers from other fish of the cod family. There are slight variations in saponification and iodine values. Our records show that pure Cod Liver Oil made under our own jurisdiction from livers of known origin had saponification value as low as 186.2 and as high as 198. The iodine value for the same oils ranged from 129.4 to 149.9.

Aloe. We find that aloe does not always effervesce with nitric acid as stated.

Rhubarb. The test for Rhapontic Rhubarb does not yield satisfactory results and will not always detect this variety. The test should be changed to conform with a similar test given in the German Pharmacopœias which yields satisfactory results. Examination under ultraviolet light will also differentiate between U. S. P. and Rhapontic Rhubarb.

Tragacanth. It appears that the sodium borate test for foreign gums needs changing. No material can be found on the market which will comply with the present test.

Alcohol Soluble Extractive. Several of these determinations such as in Sumatra Benzoin should be changed so as to give proper consideration to volatile oil and moisture content.

Fluidextract of Ipecac. The assay needs revision. It cannot be operated satisfactorily without a centrifuge.

Fluidextract of Hydrastis. The assay needs revision. It cannot be operated satisfactorily without a centrifuge.

Milk of Magnesia. The test for residue in the supernatant liquid should be changed by directing the supernatant liquid to be decanted through a washed filter.

Ether and Chloroform. It would appear desirable to determine specific gravities at 15° C. on these products instead of at 25° C.

Ether. Solid potassium hydroxide has proved more satisfactory than a solution of potassium hydroxide for the aldehyde test.

Iodides. The iodate method would appear preferable to the silver nitrate method of assay.

Heavy Metal Test. The meaning of this test as it affects acids such as acetic, hydriodic, hydrochloric, etc., should be clarified.

Sodium Cacodylate. The assay should be for arsenic instead of a titration for its alkalinity.

Tincture of Cantharides. As the drug is assayed it appears that the assay of the tincture may also be desirable.

(6) *Corrections in Wording.*

Purified Talc. The U. S. P. carries a note reading "purified talc is intended only as a filtering medium and for this purpose should not be finer than a No. 100 powder" which has since been revised to read "purified talc is intended only as a filtering medium and for this purpose should not be finer than the powder which passes through a No. 80 sieve but is retained by a No. 100 sieve." It seems that this could be made clearer by saying that the powder should not be finer than a No. 100 powder nor coarser than a No. 80 powder.

Neoarsphenamine. In Paragraph 2 in the identity test the U. S. P. says "an aqueous solution of Neoarsphenamine (1:100)* * * is not precipitated by mercuric potassium iodide T. S." This statement no doubt is based on the following taken from the 1918 Public Health Report, "Mayer's reagent does not yield a precipitate until the solution has been made acid with dilute hydrochloric acid." When potassium mercuric iodide is added to the aqueous Neoarsphenamine solution a turbidity develops followed by the appearance of a precipitate. This precipitate

is not due to precipitation of Neoarsphenamine but to the reducing action of Neoarsphenamine on potassium mercuric iodide, and the wording should therefore be corrected.

(7) *The Meaning of Statements and Definitions.*

Meaning of "Completely Soluble." One frequently finds statements of this type in the U. S. P.: "One gram of boric acid dissolves completely in 10 cc. of boiling alcohol (insoluble substances)." The statement is intended to furnish a test for the presence of insoluble substances in boric acid. It is of course clear to a pharmacist that the statement means that when this test is applied boric acid should dissolve. If strictly interpreted, however, no boric acid would comply with it because all chemicals of this type will contain traces of insoluble matter which represent what is generally termed "mechanical contamination," namely, traces of dust particles. It appears desirable to so word the test that the meaning of the U. S. P. is made more clear.

Solubilities. Under description and physical appearance, the U. S. P. in many instances gives the solubility of the substances in one or more solvents. I believe it should be made clear whether these solubility statements are to be construed merely as information or whether they are to be construed as standards with which the product must comply. In a few instances (sodium salicylate) there seem to be errors in the solubility statement of the U. S. P. This may prove embarrassing if the enforcement officers of the Food and Drugs Act should interpret these statements as standards and rule that a product not corresponding to the solubility mentioned is sub-standard.

Terms Used for Expressing Temperature. The U. S. P. IX defined terms of temperature in degrees C. but the present Pharmacopœia does not indicate what is meant by such terms as "hot," "warm," "luke warm," etc. It appears desirable that such terms should be avoided and definite temperatures substituted or that such terms be defined.

I want to make clear that the above comments represent an accumulation of notes made during the four years that the U. S. P. X has been official and that no effort has been made to determine whether others have called attention to the same items or not. This paper may therefore contain duplications of comments previously published.

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BELGIAN PHARMACEUTICAL CONGRESS.

A congress of pharmacy was held in connection with the centenary exhibition at Liege during the second week of August. At the Conference of Pharmacy held at this time the following subjects were discussed and interesting papers presented.—General Chemistry, Pharmaceutical Chemistry, Pharmacognosy, Practical Pharmacy, Colonial Pharmacy and subjects of Chemistry and Pharmacy, relating to foods, bacteriology, biology, hygiene, etc. The Congress was under the patronage of the Duke of Brabant and was organized by the professional body of the Institute of Pharmacy of the University of Liege, the Belgian Pharmaceutical Association and the Pharmaceutical Association of the Province of Liege.