Contributed and Selected

REPORT OF THE CHEMISTS' SUB-COMMITTEE ON STANDARDIZATION AND DRUG TESTING.

The General Committee on Standardization and Drug Testing have requested that we investigate methods of analysis for Elixir Lactated Pepsin, nitroglycerine, diastase and papain preparations.

Each of these problems has received our most careful attention. All of the methods herewith recommended have been tested in our laboratories. We present them to you as being the most efficient known to us at this time.

ASSAY OF ELIXIR OF LACTATED PEPSIN.

Since the different pharmaceutical houses market this preparation in various strengths, it is impossible for us to describe other than a general method. We suggest that you take of the elixir, a quantity containing approximately 0.1 gram of pepsin. Dilute this to 150 cc. with a solution of 9 cc. dilute hydrochloric acid (U. S. P.) in 291 cc. distilled water. Proceed from this point directly as outlined in the Pharmacopœia of the United States, Eighth Revision, under the Assay of Pepsin, page 335. It will be found that the other ingredients present in the original elixir will not interfere with the pepsin digestion in the dilution above recommended.

We believe the pepsin assay to be the best method of testing the activity of this elixir. However, we also strongly recommend that you estimate the alcohol contents of each and every lot, since it is advisable to verify the statements of alcohol percentage made on the label.

As you well know the methods of alcohol determination in general practice today, are still more or less inaccurate. We believe that the forthcoming Pharmacopœia is to give us an official method. This will be welcomed by all. Meanwhile we suggest that you employ the distillation-method described in Leach's "Food Inspection and Analysis," 1911 edition, page 658.

ESTIMATION OF NITROGLYCERIN.

Two determinations are necessary, one on the original supplies and the other on the finished products. There are available, two types of raw material, one an alcoholic solution and the other a trituration of nitroglycerin with some inert material such as milk sugar. Likewise the finished products are of two types, the alcoholic solution and the tablets.

Engelhardt (Journal of the American Pharmaceutical Association, 1913, page 163,) states that rather accurate results are obtained in the assay of alcoholic solutions of nitroglycerin by evaporating a measured sample spontaneously and drying the residue in a desiccator over sulphuric acid to a constant weight. We are told that this method has been approved as the official assay of the new Pharmacopœia. You will find full details on page 527, Journal of the American

Pharmaceutical Association, year 1914. You may, however, also proceed as described later under the estimation of tablets and triturations by diluting the alcoholic solution to a definite volume with ether in a manner as suggested under the "Preparation of Sample."

As you know, the Department of Agriculture has recommended two colorimetric-methods for the assay of nitroglycerin, the Modified Scoville and Modified Hay methods. For the estimation of both the original trituration used for manufacturing, and the finished tablets we can only repeat their method. We take exception, however, to their method of extraction by macerating the tablets or trituration under ether and using this ether-extract for the determination. There is no doubt but that this method will exhaust a good hypodermic tablet. However, it has been clearly proven by Dr. Thorburn of the Pitman-Moore Company and verified by Mr. Summers in the Laboratories of The Abbott Alkaloidal Company, that this method does not completely exhaust compressed tablets, granules or poorly made hypodermic tablets. It therefore seems advisable to us to recommend Dr. Thorburn's extraction-method in preference to the maceration-method.

ESTIMATION OF NITROGLYCERIN IN TABLETS OR TRITURATION.

Preparation of Sample (Thorburn Modification):—Disintegrate a quantity of tablets or trituration containing about 0.0162 gram (¼ gr.) of nitroglycerin in 20 to 25 cc. of water. Extract four times with successive portions of 25 cc. of ether. Combine ether extracts and make up to 100 cc. in a volumetric flask. Then proceed by either of the following methods.

Estimation by the Modified Scoville Method:—Of the above ether solution place 40 cc. in a carefully dried and tared 50 cc. beaker. (A second aliquot of 20 cc. may be used as a check.) Evaporate the solvent in a vacuum desiccator. Apply the vacuum gradually so as to prevent ebullition. Leave the beaker in the vacuum 30 minutes after the ether has evaporated. Weigh and calculate ether extract per tablet. Treat the residue with 2 cc. phenoldisulphonic reagent, rotating the beaker in such a way that the reagent comes into contact with the entire inner surface. After 10 minutes add water and wash into a 100 cc. flask. (If a check analysis as suggested was made, wash this into a 50 cc. flask.) Dilute to the mark and place 10 cc. (representing 1 tablet) in a 100 cc. flask, add about 50 cc. water and a few drops more potassium hydroxide solution (20%) than is required to neutralize the acid. (Do not use sodium hydroxid.) Dilute to the mark and compare the color with that produced by a standard nitrate solution similarly treated. Use any convenient colorimeter or Nessler tubes.

Reagents and Standards:—

Phenoldisulphonic Acid Reagent:—Dissolve 25 grams of pure white phenol in 150 cc. of concentrated sulphuric acid, add 75 cc. of fuming sulphuric acid (13% So_3), stir well and heat for two hours at about 100 degrees.

Standard Solution:—Dissolve .7217 gram pure KNO_3 in 1 liter of water. Evaporate 10 cc. of this solution just to dryness on the steam bath. Cool and treat the residue with 2 cc. phenoldisulphonic acid reagent, observing the precautions noted above and using a glass rod if necessary to aid the solution of the

residue. After 5 or 10 minutes dilute to 250 cc. Each cc. of this solution contains .004 mg. nitrogen. Add an excess of KOH solution to an aliquot of this solution and dilute to 100 cc. It is advisable to prepare a standard of approximately the same color as the unknown. Nitroglycerin is 5.4 times nitrate nitrogen.

Estimation by the Modified Hay Method:—Of the above described ether extract place 10 cc. in 120 cc. Erlenmeyer flask, dilute with 5 or 10 cc. alcohol and add about 5 cc. of ½% alcoholic potassium hydroxid. Cover with a watch glass and allow to stand 10 minutes. Place on steam bath, allow to boil, remove the watch glass, and when most of the liquid is evaporated, add about 25 cc. water and leave on steam bath until the odor of alcohol can no longer be detected. Cool and dilute to 250 cc. Each cubic centimeter of this solution represents .01 of a tablet. Introduce 5 cc. representing .0324 milligram nitroglycerin into a 100 cc. graduated flask, dilute with sufficient water to make the volume 90 to 95 cc., add one drop concentrated hydrochloric acid, then 2 cc. sulphanilic acid solution and 2 cc. napthylamine hydrochloride solution. Complete the volume with water. Prepare at the same time and in the same way, standards containing known amounts of sodium nitrite, by taking 80 cc. of the standard solution of sodium nitrite, and adding one drop of concentrated hydrochloric acid, 2 cc. sulphanilic acid solution and 2 cc. napthylamine hydrochloride solution, and completing volume to 100 cc. with water. Stopper the flask and mix well. Compare the colors after 30 minutes, each cc. is equivalent to .00064 mg. nitroglycerin.

Reagents and Standards:—

Sulphanilic Acid Solution:—Dissolve 1 gram in 100 cc. of hot water.

Napthylamine Hydrochloride Solution:—Under a hood boil .5 gram of the salt with 100 cc. of water for 10 minutes, keeping the volume constant. Filter and keep in a glass-stoppered bottle.

Standard Solution of Sodium Nitrite:—To a cold solution of about 2 grams of sodium or potassium nitrite in 50 cc. of water, add a solution of silver nitrate as long as a precipitate appears. Decant the liquid and thoroughly wash the precipitate with cold water. Dissolve in boiling water. On cooling the silver nitrite is precipitated. Dry the crystals in the dark at the ordinary temperature (preferably in a vacuum). Weigh out 220 milligrams of the dry silver nitrite, dissolve in hot water and decompose with a slight excess of sodium chloride. When the solution becomes clear, dilute to 1 liter. Dilute 5 cc. of this solution to 1 liter. This second dilution is the standard to be used. It contains 0.0001 mg. nitrite per cc.

Only nitrite free water should be used in the estimation by the Modified Hay method.

Of the above methods the Scoville is more generally employed because of the rapidity with which it can be operated. It is to be remembered, however, that both of the above methods involved a colorimetric comparison, and that different operators are better able to judge one color in preference to another. As you well know, the Scoville method gives a yellow-colored solution while the Hay method yields a rose-colored solution. We suggest, therefore, that you try both methods on a known standard and then adopt the one that gives the most consistent results. So far as accuracy is concerned, outside of the end color comparison neither method is to be preferred over the other.

This committee most emphatically reiterates Mr. Baker's statements to you of a year ago that nitroglycerin tablets when properly bottled do not deteriorate on standing. During the past year, we have tested monthly a specimen lot of tablets. These tablets are to-day as potent as they were one year ago.

All that is necessary is to devise a method of manufacture which will give a product true to label, then bottle properly.

DIASTASE.

As you all probably know, diastase is to be official in the forthcoming Pharmacopœia. We are also to have an official method of assay. The provisional method has already been described on page 15 of Part 1, First Proof, United States Pharmacopœia, Ninth Revision.

As Mr. Baker of the Norwich Pharmacal Company, has closely studied this method for the committee, we deem it best to quote his complete report on this subject.

"Comparison and Criticism of Two Methods for Determining the Starch Converting Power of Diastase."

"I will represent the method proposed for the pharmacopœia, ninth revision, as method (a) and the method used by the N. P. Co. as method (b). This method is taken from, but slightly modified, to the one adopted by the Council of Pharmacy, A. M. A., as printed in the Journal A. M. A., Vol. 51, No. 2, Page 142.

"Method (a) is as follows: Mix a quantity of potato starch which has been purified as described under Pancreatinum, equivalent to 5 gm. of dry starch, in a beaker with 10 cc. of cold distilled water. Add 140 cc. of boiling distilled water, and heat the mixture on a water-bath, with constant stirring for 2 minutes, or until a translucent uniform paste is obtained. Cool the paste to 40° C. in a water bath previously adjusted to this temperature and add a solution of 0.1 gram of Diastase in 10 cc. of distilled water at 40° C. just previously made. Mix well and maintain the same temperature for exactly 30 minutes, stirring frequently, when a thin, nearly clear, liquid should be produced. At once add 0.1 cc. of this liquid to a previously made mixture of 0.2 cc. of tenth-normal iodine V. S. and 60 cc. of distilled water. No blue nor reddish color should be produced.

"Method (b). A clean grade of potato starch is thoroughly washed and carefully dried at a low temperature and finally at a higher temperature to about a 10% moisture content. The exact moisture content to be determined in a separate experiment. For the test enough of the starch is taken (about 11 gms.) to make to 500 cc. of an exactly 2% (anhydrous) starch content. The boiling of the paste should be continued for 10 minutes with constant stirring to keep from burning. For each test quantities of exactly 25 gms. of the paste are weighed in a series of 250 cc. flasks placed in a water-bath and kept at a temperature of 40° C. The Iodine test solution is made by dissolving 2 gms. of Iodine and 4 gms. of Potassium Iodide in 250 cc. of distilled water, 2 cc. of this solution is then diluted with pure water to make 1000 cc. The diastase solution is made by dissolving or suspending 0.2 gms. of diastase in 100 cc. of distilled water. The solutions are used in the following way: Definite volumes of the solution are added to the different flasks containing the starch solution and the mixtures are well shaken. The volumes added may be as follows: 4 cc., 4.5 cc., 5 cc., 5.5 cc., 6 cc. In eight minutes tests are begun by removing volumes of 5 drops from each of the digesting mixtures by a pipette and adding this to 5 cc. of the dilute Iodine solution in a clear white tube standing over white paper. If at the end of 10 minutes drops from one of the flasks fail to give the Iodine reaction, we are ready for the more accurate test; for example, the flasks containing 5 cc. diastase solution did not respond to the Iodine reaction, but the one containing 4.5 cc. did, then a second test would be carried out under exactly the same conditions as the former using 4.6, 4.7, 4.8, 4.9 and 5 cc. diastase solution to 25 gms. of the starch paste. The diastase solution must be of the same temperature as the starch paste. The test is carried to the loss of all color. The diastase solution should have been just previously made and, if working for any length of time, fresh solutions should be made from time to time, as aqueous solutions of diastase are very unstable and soon lose their power of conversion. The dilute Iodine solution should not be put in the tubes until just before it is needed.

"A good diastase will convert at least 50 parts of starch to a colorless end point in 10 minutes. While this method is a 10 minute and the other method a 30 minute one, both methods checked on the diastase under examination as the following figures will show.

Method (a)			
Diastase parts.	100% starch to colorless end point parts.		Time.
" 1	"	40	10 minutes
" 1	"	50	15 "
" 1	"	55	22 "
" 1	"	60	30 "

Method (b)			
Diastase parts.	100% starch to colorless end point parts.		Time.
" 1	"	40	6 minutes
" 1	"	50	8 "
" 1	"	60	10 "
" 1	"	70	13 "

"The fact that the 10 minute method gave the same results as the 30 minute method is due to the vast difference in the strength of the Iodine solutions used. In method (a) we have 0.00254 gms. of Iodine in 60 cc. of water, while in method (b) we have but 0.00008 gms. in 5 cc. We, therefore, have 32 times more Iodine present in method (a) than in (b) and this will give a reaction with the starch diastase solution when the weaker one will not. This condition exactly counteracts for the difference in time for the two methods.

"Method (b) has a few important advantages over the one proposed for the U. S. P. 9th revision. The first and most important point is that when the starch paste is once made, twenty tests may be made from the 500 gms. With method (a) we are using a cumbersome amount of starch paste for each individual test and the test simply shows whether or not the sample tests are up to the U. S. P. standard and to find the exact value of the diastase will require probably several tests, which will make a very tedious task, making and cooling such large individual quantities of starch paste and the individual weighings of the diastase and also the longer period of time for each test.

"The second important point is the end point for the two methods used. In method (b) the end point is very delicate and cannot be mistaken as 5 cc. of the dilute iodine solution in a Nessler tube appears nearly colorless, and any blue, red, or yellowish color which may be produced can be detected with sufficient accuracy. In method (a) the solution is quite highly colored with free Iodine. The directions state to add 0.1 cc. of the starch diastase solution to the 60 cc. of the Iodine solution and no blue or reddish color should be produced. While there are no instructions calling for this, a careless or thoughtless worker might shake the tube slightly and disseminate a red color that is actually produced, so that it would be impossible to be detected. This allows a chance for a sample to be reported up to standard when possibly the starch is only taken to the dextrose or maltose stage.

"Both methods call for potato starch. While potato starch will give a higher value for diastase, and this may seem as a case of lowering standards instead of raising them, I am in favor of its use, because of the physical characteristics of the two. I have always been able to prepare a much more uniform paste from potato starch than from corn starch and would prefer raising the standard to 1/60 or 1/70 and still use potato starch."

The above discussion comparing Mr. Baker's modified method to the proposed pharmacopœia method is entitled to your profound consideration. As has been pointed out, Mr. Baker's method enables you to easily determine the exact strength of your diastase, while the proposed method for the Pharmacopœia is little more than a qualitative method. We believe that this Association should adopt Mr. Baker's assay for their official method. We also deem it advisable for the Association to send a copy of Mr. Baker's report to Prof. Remington, Chairman of Revision Committee, for his further consideration as a better method for the new Pharmacopœia, for it is well to remember that no matter how poor a method may be, should it be included as the official method in the forthcoming Pharmacopœia, the Association members will be compelled to adopt it in their laboratories. The time has come when the Pharmacopœia has become a legal standard rather than a pharmaceutical guide.

PAPAIN.

The final subject for consideration assigned to us by the General Committee is the assay of papain. This is indeed a difficult task.

There is considerable difference of opinion among the various authorities not

only upon the media to be employed but also the substance to be digested. It appears that papain contains vo distinct enzymes—one acting in acid and the other in alkaline media. Arguments have also been advanced in favor of testing papain not only on raw beef but also on blood fibrin or egg albumin. It is our opinion that raw beef is the best substance for this purpose, since it more nearly duplicates in the laboratory the function of papain in the body.

Graber (Journal Industrial and Engineering Chemistry, 1911, Page 921), has shown that papain is most active in acid-solution, neutral media ranking second and alkaline media, third. While this may be true, the testing of papain in acid solution does not eliminate an adulteration with pepsin. It has been found in the Laboratories of The Abbott Alkaloidal Company, that a 5% adulteration with 1/10,000 pepsin would give an otherwise inert papain an activity of 1/30, when tested in acid media. The true question is "how does the papain react in the body?" If it digests fibrin best in acid solution, it will perform this function in the stomach and not in the intestine as is now maintained by some. We should, therefore, devise some method that will eliminate adulteration with pepsin and still show the active power of the papain in acid solution.

A method now in vogue for testing papain in acid media is that of Graber, described in the Journal of Industrial and Engineering Chemistry, 1911, Page 921.

As a method for assaying papain in alkaline media we recommend the following, devised by Mr. Baker. It is conducted as follows: "The test is 1:30 in 6 hours at 50° C. That is, one part of papain should in 6 hours at 50° C. so completely digest and disintegrate 30 parts of raw beef that the undigested residue should not measure more than 2 cc. using 10 grams of beef for each experiment. The test is conducted on round steak free as possible from fat and gristle, which has been finely minced by passing through a meat chopper. For each test 10 gms. of beef, 100 cc. of distilled water made slightly alkaline to litmus with sodium carbonate, .3 gm. of ferment. Invert bottles once every 10 minutes as per U. S. P. test for pepsin. Pour in tall graduated cylinder at the completion of the assay."

While we have called to your attention these two methods, yet we most strongly recommend the following promising method proposed by Mr. Thorburn. This method is both unique and ideal in that it not only tests the papain in both alkaline and acid media, thus giving the total digestive activity, but also eliminates the possibility of adulteration with pepsin; as the pepsin, if present, is destroyed in the preliminary digestion. This method appears to us to be the best yet proposed for the assay of papain. The method is herewith quoted from Mr. Thorburn's report to the committee.

"Dissolve papain .400 gm. and sodium bicarbonate .750 gm. in distilled water enough for 100 cc. Heat to 50° to 55° C.

Scrape lean round steak (better results are obtained by scraping the meat to a pulp instead of grinding) rejecting gristle, fat, etc., to a pulp; weigh 10 gm. meat pulp and place in a 200 cc. digestion-flask; add 100 cc. of the warm solution of papain and sodium bicarbonate. Digest for four hours, shaking the mixture once every 10 minutes; then pour into a measuring cylinder and let stand at rest for one-half hour. If the digestion flask is fitted with a stopper carrying a small graduated tube it is of course much more convenient than pouring into a cylinder; in this case invert the flask and read after one-half hour's standing.

A blank digestion of the meat pulp with sodium bicarbonate should be carried along with the papain digestion.

Not more than 10 cc. of residue should remain after the alkaline digestion with papain.

After reading this residue, warm the mixture to 50° to 55° C. and add concentrated hydrochloric acid 1½ cc.—sufficient to neutralize the alkali and leave .2% to .3% of free acid.

Again digest for four hours shaking every 10 minutes. Let stand at rest one-half hour, then read the residue which should be less than three cc.; this gives the total digestive power of the papain as 1 to 25 four-hour tests which compares favorably with a 1 to 30 six-hour test."

It occurs to us that you would welcome our calling to your attention those drugs and chemicals that each of us have found deficient during the past year. We do this to impress upon you the importance of testing all your supplies, and also the fact that the label or brand is no criterion to purity. Each and every member of this association should at least test all crude supplies. We recommend this not only for your individual welfare but also for the good of the profession. You should also check-test your finished products. You should all attain that position where you can state that your goods absolutely conform to the label, in that they contain the exact quantity of the best obtainable drug as thereon stated. To do this you must invoke the services of the pharmaceutical chemist.

Mr. Baker reports the following as a list of crude drugs and chemicals rejected at the chemical laboratory of the Norwich Pharmacal Company during the past year.

Alum, dried	Continued marked quantities of material insoluble in water.
Ammonium Carbonate	Badly decomposed.
Benzoin	Three different lots rejected, all deficient in alcohol-soluble contents.
Balsam of Tolu	Deficient in alcohol-soluble content.
Balsam of Tolu	Contained rosin.
Black Haw	Not true Black Haw but so-called Variety Black Haw.
Short Buchu	A large percentage of stems present.
Chloroform in bottles of 100 gms.	Shortage in weight of contents, varying from 68.7 gms. to 94 gms.
Cinchonine Sulphate	Melting point low and chloroform-soluble deficient.
Calcium Hypophosphites	Solution in water decidedly opaque.
Coca Leaves	The leaves had deteriorated badly, odor musty, ether-soluble alkaloids but .09%.
Calcium Glycerophosphates	Contained appreciable amount of chlorides.
Calcium Glycerophosphates	Contained an appreciable quantity of citric acid.
Calcium Carbonate	Two lots, aluminum in excess the U. S. P. limits.
Cannabis American	Resin content low 6.5%.
Cayenne Pepper	High in ash content, total ash 9.86%. HCl insoluble ash 5.6%
Chlorophyll	Odor very disagreeable.
Cresol	Gravity low, insoluble in water as it contained tarry matter.
Hops	Rejected, as they were inferior in both color and odor.
Henbane	Assayed .15% mydriatic alkaloids which was suspiciously high
Iron Peptonate	Assayed 20% Fe^2O^8, label claimed 25%.
Iron Peptonate	Rejected on odor.
Iron Sulphate, dried	Gave moisture content of 33%.
Gelatine	Three lots rejected on account of color.
Gentian Powd.	Adulterated with foreign material.
Glycerine	Contained sulphates and color not up to standard.
Glycerine	Color not up to standard.
Guaiac	Four lots, rejected, low in alcohol-soluble content, high in ash content.
Lard	Two lots rejected on odor.
Lithium Citrate	Did not conform to the U. S. P. in purity test.
Lupulin	Five lots rejected—ether soluble content deficient—ash content high.
Licorice Root	The extract obtained had a musty taste.

Lobelia	Rejected as it was mostly stalk and but very few leaves.
Manaca Root	Spurious variety.
Mentha Piperita	Inferior in both color and odor.
Po. Gum Myrrh	Ash content high 15%.
Magnesium Sulphate	Contained the heavy metals in excess of the U. S. P. limits.
Magnesium Sulphate	Purity not up to U. S. P. standard—color also inferior.
Magnesium Oxide heavy	Contained excess of calcium.
Nux Vomica	Physical appearance of the seeds was poor—strychnine content 1.222%.
Oleic Acid	Congealing point 14° C., which is high. Notable quantities of palmitic and stearic acids present.
Oil Thyme	Color very dark.
Russian White Oil (Liquid Petrolatum)	Two lots rejected on account of turbidity.
Phenol	The crystals were off color, being quite red.
Peptone from Beef	Proteid content 71%, which is below our standard.
Pareira Brava	Spurious variety.
Paraffin	Tastes strongly of mineral oils.
Podophyllin	Two lots rejected, deficient in alcohol-soluble content and high in ash content.
Potassium Hypophosphite	Solubility in water not in accordance with the U. S. P.
Peroxide of Hydrogen	Assayed 2.8% H^2O^2—contained free acid and total solids in excess of the U. S. P. limits.
Pink Root	Contained a large amount of earth and dirt.
Gum Senegal	Contained too large an amount of wood.
Squaw Vine	Inferior in physical appearance.
Strophanthus Seeds	Very damp and musty.
Strontium Salicylate	Two lots rejected as color was decidedly pink.
Zinc Oxide	Two lots below U. S. P. standards for purity.
Zinc Valerianate	Two lots below U. S. P. standards for purity.
Vinegar	Gravity and acidity below N. Y. State requirements.

Mr. Thorburn has enclosed the following memorandum to illustrate the need of analytical work as a control in drug compounding. He states that "We have tabulated the last one hundred samples submitted to the scientific department by the manufacturing departments. These samples represent forty-six different preparations and involve about twenty different kinds of determinations such as the estimation of arsenous acid, ammonia, alkaline hydroxides, pepsin, iodine, iodides, lead, ethyl nitrite, phosphoric acid, hydriodic acid, jalap resin, alkaloids from aconite, gelsemium, ipecac, nux vomica, opium, pilocarpus, belladonna, henbane, stramonium, and extractive from various drugs.

"Of these one hundred samples fifty-one were below standard strength, thirty-two complied with the official standard and seventeen were above standard.

"Some extreme cases of deficient strength are worth noting; 2 samples of Fld. Ext. Berberis were 60% and 67% below; 2 Stramonium preparations were 50% below; Fld. Ext. Hyoscyamus varied from 13% to 39% below; Solution Iodine Compound was 47% below; 1 sample of syrup Hydriodic Acid was 50% below; Fld. Ext. Nux Vomica varied from 1% to 19% below and from 2% to 20% above; Fld. Ext. Gelsemium was 48% and 55% below.

"Few of the samples that were above strength were more than 10% above but Extract Belladonna Leaves finished 55% above standard. A number of Pepsin digestion tests gave very satisfactory results but in several cases these samples were more than 25% below standard.

"This series of samples is good evidence that no scheme or plan for the manufacture of pharmaceutical preparations is complete unless it includes the analytical testing of the article after it is compounded and most important of all, its adjustment to standard."

The Abbott Alkaloidal Company report having rejected the following supplies:

Aconite	Low in alkaloidal content.
Alcohol	Excess organic impurities.
Alum	Excess iron.
Apomorphine Hydrochloride	Excess moisture.
Arsenous Acid	Insoluble matter.
Barium Sulphide	Two shipments purity but 19 to 22%.
Calcium Chloride	30.9% water.
Calcium Carbonate	Chlorides.
Chloral Hydrate	Low melting point. Chlorides.
Corn Oil	Less than content.
Diacetyl Morphine Hydrochloride	Excess water.
Hydrastinine Hydrochloride	Excess water.
Ipecac	Low alkaloidal content.
Lanum Hydrous	Moisture.
Methylene Blue	Ash.
Milk Sugar	Insoluble matter.
Morphine Hydrobromide	Excess water.
Nux Vomica	Low alkaloidal contents.
Oil of Cajuput	Copper.
Oil of Peppermint	Dimethyl Sulphide
Papain	Digestive activity.
Potassium Permanganate	Chlorides. Sulphates.
Sodium Bisulphite	Moisture.
Sodium Silicofluoride	Purity.
Strophanthin	Reduced alkaline cupric tartrate in cold.
Talc	Iron.
Tartaric Acid	Sulphates.
Silver Oxide	Silver Chloride.
Zinc Valerate	Purity.
Sodium Salicylate	Alkaline to litmus.

We call your attention to "A Bibliography of the Deterioration of Drugs and Pharmaceutical Products" by E. G. Eberhardt and F. R. Eldred, Indianapolis, Ind., published in the January issue of the Journal of the American Pharmaceutical Association, 1914; and to the "Purity of Chemicals and Drugs" by H. Englehardt, published in the Journal, 1913, page 163.

We also recommend that you submit all compound formulas to your chemists for their approval. Such a procedure will assure you of having formulas already supposedly therapeutically balanced, further improved by their chemical and pharmaceutical adjustment. All three considerations are necessary to secure an elegant and scientific preparation.

In concluding this report the committee desire to herewith acknowledge to the Association their appreciation for the honor that has been conferred upon them through their appointment to this office.

The chairman likewise desires to thank both Mr. Baker and Dr. Thorburn for their prompt and hearty coöperation in the preparation of this report. Both of these gentlemen have herewith suggested to you, methods that are not only unique but also far superior to those in general practice today.

Franklin Peale Summers,
A. D. Thorburn,
W. L. Baker.