

REPORTS OF COMMITTEES

ABSTRACT FROM THE REPORT OF THE COMMITTEE ON TRADE INTERESTS,
PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.

BY MR. HARRY B. FRENCH, PRESIDENT OF SMITH, KLINE & FRENCH CO.

MR. E. B. PRITCHARD, *Chairman*:

During the year preceding the report presented to the Thirty-eighth Annual Meeting in 1915, the same conditions have influenced the drug market as prevailed during the previous year, and these conditions are of an abnormal character, because of the continuance, during these years, of the European War. The prices of both crude drugs and chemicals continued to climb during the Fall of 1915. The abnormal heights reached were due in part to speculation, in part to feverish haste in buying, and in part to the ignorance or lack of knowledge of the buyers as to sources of supply.

During the last few months, however, there has been a decided change for the better, especially as regards chemicals. The buying apparently has been concentrated to a few and able hands. The primary markets have been sought and therefore to a certain extent the speculator has been eliminated, and finally the production of chemicals along certain lines has greatly increased in this country. The result has been, so far as regards chemicals, that speculators have become very much frightened, especially as there has been considerable talk of peace. They have had visions of the "writing on the wall," and, therefore, they are each trying to get ahead of the other in disposing of their stocks. The losses in many instances are quite heavy, and even at greatly reduced prices a market is not readily obtainable. It is difficult, if not impossible, to force the sale of goods for which there may not be an active demand, and which, although offered at very much lower than the supposed market prices, are still very much above the normal.

There are many, and we are inclined to agree with them, who think that another opinion may justifiably be held as to future conditions. Many thinkers believe that peace is not possible for a long time to come; their conclusions are, Germany will not accept such terms as the Allies are willing to offer, until the latter have shown military superiority. If, then, the war is to continue, as was predicted by Lord Kitchener, for three years, it means that this terrible struggle will probably still be going on in the latter part of the year 1917. It is with the utmost reluctance that men base their business operations on the continuance of a bloody struggle of this character, but it is necessary to take all circumstances into consideration in forming opinions and deciding upon actions. The present period of declining prices, which has been in force for the last three or four months, and has been accentuated during the last six weeks, is being prolonged by the fact that it is impossible to ship goods to Russia, for the reason that all available space, for shipments to Archangel, has been taken up, upon the opening of navigation, by the Russian Government in order to replenish their imperative wants. It is believed, however, that there will be space available early in July and that there will be large shipments to that important buyer. It therefore might happen that weak speculators may have considerably reduced their holdings, and there may arise a large demand for chemicals and a very small supply be found.

The effect of this war on botanicals was not so pronounced at first, but as time went on the shortage produced by the cutting off of some products from the commerce of the world became greater and greater. The questions of finance and transportation also played their parts. Nearly all stocks of botanicals that were bought before the war have been exhausted, and it is to be feared that the imperative needs of manufacturers during the next twelve months will be but imperfectly filled from the accessible sources of supply.

The great corporations, having hundreds of millions invested in steel, were slow in taking up the question of the utilization of the waste from their coke ovens, especially as this involved a very heavy expenditure of money in changing those coke ovens so as to ad-

vantageously secure the waste. When the work was undertaken, it was pushed forward vigorously and the production is now on a very large scale. This has already seriously affected the price of phenol, which is now procurable in a large way, in the form of white crystal, U.S.P. quality, at 75 cents per pound. It will also at a later time increase the production and lower the costs of all those products belonging to the numerous lines that are obtainable from the waste of coke ovens, and that are important enough to justify the investment of capital necessary to develop them.

One of the products, however, that does not seem to have engaged proper attention, or, if it has, the investigation has not been successful, is benzoic acid *ex* toluol. A couple of years before the war an importation was made into this country of some 40 tons of benzoic acid *ex* toluol at a laid-down cost, duty included, of about 19 cents per pound. The nominal market price to-day is \$7.25, and it would not be possible to buy 5000 pounds of benzoic acid in the United States to-day at any price. The season is now coming on when there will be a great demand for sodium benzoate, and it looks as if considerable difficulty might arise in furnishing the necessary supplies.

Shipments to this country and to other countries in 1915 of citrated lime were very large, in fact, much larger than normal shipments. The capacity of the manufacturers for making citric acid has not been, we think, considerably enlarged and therefore, although working their capacity to the utmost, they have not been and will not be able to fill the speculative demands that were made upon them. The American manufacturers, however, have steadfastly pursued the policy of limiting their deliveries to their regular customers for their normal supplies, and of late have been demanding a guarantee that the goods, so delivered by them, shall not be exported from this country. It unfortunately happens at times that conditions, such as these, are accepted and evaded by selling to a third party, who will turn it over to a fourth party, who exports it. It is recognized, of course, that this method is an indirect way of violating an agreement. The manufacturers' price to-day is 67 cents per pound, which is about 25 cents above a normal price. The price for export varies from 75 to 80 cents per pound, with very little obtainable for that purpose. The earlier part of this year citric acid was sold for export, as high as \$1.00. We may venture to make the statement that citric acid will be obtainable for all legitimate wants in this country at the existing price of 75 cents per pound, in barrels.

Quinine during the height of speculative excitement last fall sold as high as \$2.50 per ounce in a small way and \$2.25 per ounce in a large way. Many hundreds of thousands of ounces changed hands. Every holder who had a small stock, throughout the country, rushed his goods to the market to take advantage of these extraordinary high prices. Towards the end of the year and the beginning of the present year, owing to the re-organization in the methods of buying, the placing of orders at Rotterdam and Amsterdam with first hands greatly decreased the foreign demand and quinine began gradually to decline. Later, in 1916, the decline became more rapid, although in the meantime manufacturers in this country had advanced their price to 75 cents per ounce, as the cost of bark had increased. In the meantime, the stock of quinine in London had been cut down to about half of what it was a year ago, and, if the use of quinine continues on as large a scale, it looks as if at the end of 1916 the stock of quinine in London would become so reduced as to be no longer of importance. In the meantime, holders of considerable stocks of quinine, who had thought that there was no roof to the price, have been pressing their product on the market and we have been told that offers have been made at a price as low as 50 cents per ounce. The manufacturers' price continues to-day at 75 cents in 100-ounce tins. It must be remembered that it was customary to import into this country several million of ounces of quinine from Germany every year, and while there have been importations of quinine since the war, they have been of comparatively small amounts. Taking also into consideration the advanced cost of bark, and the produced stocks in London, it would not be surprising if the necessities of the warring nations, compelled to again go into the markets of the world for large amounts of quinine, might force very much higher prices.

U.S.P. alum, with potash base, was for a long time almost unobtainable, but during the past year large shipments have been brought from Japan, which country is now producing an increasing number of chemicals. The present price of powdered potash alum, U.S.P., in

barrels, is $8\frac{1}{2}$ cents per pound, as compared with $5\frac{1}{2}$ cents per pound for ammonia alum. We understand that ammonia alum will be official in the next Pharmacopœia.

Antipyrine was imported before the war in large quantities at something less than \$2.00 per pound. During the past year it advanced to as high as \$60.00 per pound. It is now in somewhat better supply and can be obtained in quantity at about half that.

The demand for caffeine alkaloid has been very large. Certain manufacturers must have it, whatever the cost, and it has sold as high as \$18.00 per pound, in quantity. It seems somewhat extraordinary that this is so, because tea fluff, from which caffeine has been manufactured, has not advanced proportionately. The explanation probably is, that there are but few manufacturers of caffeine and they have taken a natural advantage of the market conditions and the large export demand.

Owing to the large export demand, and the high cost of its base material, chloroform was advanced at one time to 70 cents. This has been followed by a reaction and, at this writing, the manufacturers' price in 1000-pound drums is 50 cents per pound.

Epsom salts at one time advanced so largely that it sold at 7 cents per pound in England, and thereafter could be exported from this country at a handsome profit. The market price to-day in barrels is $3\frac{1}{4}$ cents per pound for the U.S.P. quality.

Years ago a very fine quality of asafetida could be bought for as low as 10 cents per pound. In order to increase their profits, the natives of Southern and Central Asia, where the drug is gathered, began to ship stones and dirt with a small admixture of asafetida. On the enactment of the Federal Food and Drugs Act in 1906, the law began to be enforced, requiring that the ash content of the asafetida should not be over 10 percent and that its solubility should be 50 percent or over. For a long time it was very difficult to get asafetida of this quality, but finally the market adjusted itself to those conditions, though it considerably advanced the price. Recently, however, there have been no shipments from the primary market, owing to conditions due to the war, and to-day hard asafetida is worth \$1.00 to \$1.10 per pound, in quantity. There are no immediate prospects of relief.

Lycopodium is one of those Russian articles that is at the moment almost unobtainable. Before the close of navigation in 1915, it was reported that two hundred ships left Russia, but were caught in the ice pack and only began to arrive some time in May. Large quantities are afloat on these vessels. The stock of lycopodium at the moment in this country is exceedingly small and it cannot be obtained in large quantities. For such as is procurable, \$4.00 is asked.

The same remarks apply to Russian cantharides as to lycopodium and at this writing pure powdered Russian cantharides would bring \$8.50 per pound.

As is well known, the price of all potash preparations has been very seriously advanced, because of the inability to obtain muriate of potash from Germany. The production, however, of potash in the United States is advancing. Certain enterprising citizens are gathering kelp on the coast of California; as ingenious machinery has been invented, and are now producing potash of satisfactory quality on an increasingly large scale. In due time we shall be able to supply a large portion of the demand and we hope the producers will be given sufficient protection so to prevent their industry from being destroyed at the termination of the war.

Licorice is very largely used in plug tobacco. The largest supply of the root formerly came from Mesopotamia. As our readers know, there has been severe fighting in that region between the two rivers—Tigris and Euphrates—and the region throughout there, and shipments have been practically stopped. The large manufacturers in this country are accustomed to bring this root in shipload lots, and it is found now very difficult to obtain sufficient supplies from other sources. It is thought that in a few months arrangements may be made whereby shipments may be had from Russia, which will relieve the situation. In the meantime the root and the extract of the root have very largely advanced in price, the advance being from 200 to 300 percent.

Sugar of milk at this writing is very difficult to obtain in sufficient quantity for the ordinary demands of this market. This is due to the fact that the largest manufacturing establishment was practically destroyed by fire, and because it is impossible to import milk sugar from Holland. We believe that when the factory that was burned down has been

rebuilt, the position will be very much improved, although we can scarcely expect normal prices for milk sugar until after the war.

Owing to the very heavy advance in the price of sugar and the heavy demand, saccharin has very largely advanced in price, until to-day \$15 is a fair price, in quantity.

Among the important chemicals that have sold at very high prices are salicylic acid and sodium salicylate. Thousands of pounds were shipped from this country and sold in England as high as \$4.00 per pound. During the past year statements have been made repeatedly that supplies would be increased, and, therefore, we might expect very greatly reduced prices. As a matter of fact, during the last few months prices have slightly declined, because the foreign demand has been somewhat reduced, but there is apparently now a revival of such demand and we may expect for the next few months that prices will be firmly maintained. The manufacturers have continued to supply their customers in very moderate quantities at about \$2.50 per pound.

On account of the very large export demand, the manufacturers of borax in this country have found it necessary to advance their price and are very much behind in their deliveries.

Paris green has been very greatly advanced because of the increased cost of blue vitriol, of which about two pounds is used to one pound of Paris green, and the increased cost of arsenic. It is probable that only small quantities have been laid up in stock by the manufacturers, and if there is a large demand this year, it may be found that it will be difficult to fill the orders.

Blue vitriol at one time sold as high as 22 cents, but recently manufacturers have offered carload lots at 15 cents per pound.

The United States Government now places very stringent regulations upon the importation of cannabis indica, following the policy of the English government, who levy a heavy tax of about \$1.50 per pound on every pound produced in India. It is rather interesting, however, to know that the government is encouraging the cultivation of cannabis indica in this country.

Mercury has had a very interesting career. The normal price is about \$38 per flask. The early part of this year it advanced to \$325 per flask because of the demand by the manufacturers of ammunition. As it was found impossible to obtain sufficient supplies of this in the open market, an arrangement was made by the British Government, for whom the munitions were being manufactured, to permit the sale by English holders to American manufacturers of munitions. As this has lessened the market demand, the price in a few weeks declined from \$325 to about \$80 per flask. Mercurials advanced and declined proportionately.

Glycerin advanced as high as 70 cents, but is now selling at about 55 cents per pound.

Dalmatian insect flowers are not obtainable. Japanese insect flowers, however, are of equal quality and can be obtained of 100 percent purity powdered, at about 45 cents per pound.

Naphthalene has largely advanced, and at one time this year the largest manufacturer in this country refused to accept further orders. The present market price in barrels is 13 cents per pound.

Norwegian cod liver oil was bought up by the German Government and the price advanced from a normal price of \$20 per barrel to \$160 per barrel.

Cut dog-grass is not an article of importance but it seems to be needed by certain parties in this country. The price advanced from a normal price of about 10 cents per pound to \$1.50 per pound for the fine cut.

Imported hellebore root is almost unobtainable. A normal price is about 8 cents and the present price for powdered is about 45 cents per pound.

Salol advanced at one time to about \$12, but is now being manufactured in increasing quantities in this country and is steadily declining.

Zinc oxide, U.S.P., advanced from a normal price of 8 cents to 35 cents per pound, but it has now a declining tendency, and we may expect lower prices from now on.

SUB-COMMITTEE REPORT ON U. S. PHARMACOPŒIA.*

On the eve of changes, additions and deletions in our official standards such as occur when a new pharmacopœia becomes official, it does not seem advisable to bring forward a lengthy report from the Chemists Sub-committee. U.S.P. standards are for all practical purposes part of the law of the land and when they require attention other matters must wait.

The ninth revision of the United States Pharmacopœia is practically ready for distribution and will, we are told, become official September 1, 1916.

Most of our members who are accustomed to have their products in use in the treatment of disease within a few days, or, at the most, a few weeks after compounding, will find this interval between date of issuance and date of becoming official—about three months—long enough to familiarize themselves with the more important changes and added requirements. Nearly all of our members in respect to the time required for changes are in much better position than houses most of whose products go through two, three or four stocks before reaching the person who controls their use by the consumer. It is advisable that every member procure immediately a copy of the new pharmacopœia and scrutinize it closely and then make at once any changes that may become necessary in stock or labels. The changes in chemical tests, assays and standards as made by the new book are rather numerous.

One change that is of very general interest is the introduction of the word "mil" as a new name for what has heretofore been called "cubic centimetre." The term "cubic centimetre" is discarded: we urge that our members be among the first to introduce this new term to our medical friends: just write or speak of "mils" instead of "cubic centimetres" and the change is made. The pharmacopœia will also give an official abbreviation for many of its titles: this desirable addition should be used at every opportunity.

Another feature of interest is the listing under crude drugs of the preparations containing that drug.

A chapter on sterilization is included in Part II of the new book. A more general use of sterilization in making pharmaceutical preparations will increase materially the standing and reputation of these articles in the eyes of the latter-day physicians.

Our meeting can with profit give considerable time to a discussion of the new pharmacopœia.

Since there will be considerable interest manifested in drug and medical circles in the new revision it is desirable that our members act promptly in giving our medical friends correct and concise information concerning these changes, additions and deletions. Our association may well consider preparing a booklet giving such information for distribution by our members.

ASPIRIN.

A large quantity of inert mixtures of powdered substances such as milk sugar, alum, salicylic acid, starch, etc., have been sold during the past year as acetyl-salicylic acid either in powder or in tablets.

Through the efforts of the drug inspectors of the Bureau of Chemistry the market has been largely cleared of this fictitious article, but it must be remembered that continued watchfulness is the only safe procedure.

Mr. J. P. Snyder of the Norwich Pharmacal Company presents the following identity and purity tests and your committee recommends very close scrutiny of all purchases of aspirin.

TESTS FOR ASPIRIN.

At present, a careful examination of this chemical is essential, as the scarcity of the product, and the corresponding high price, has made it liable to adulteration by unscrupulous manufacturers.

Acetyl-salicylic acid is prepared commercially by treating salicylic acid with an excess

* Presented at ninth annual meeting of American Association of Pharmaceutical Chemists, Cedar Rapids, Ia., June 1, 1916.

of acetic anhydride at 150° C. under a reflux condenser. It occurs in colorless crystals and in a white crystal powder; is odorless and has a sweet taste.

Identity Test—1 gramme of aspirin boiled with 10 Cc. of a 10 percent sodium hydroxide solution for two minutes will yield a white precipitate upon addition of sulphuric acid. This precipitate should, after thorough washings, have a melting point of 157° C. and should answer the ferric chloride identity test of the U.S.P. VIII., for salicylic acid. The filtrate from the salicylic acid should have a strong odor of acetic acid. The melting point of aspirin appears to vary more than is customary with organic chemical compounds. Emery and Wright, of the Association of Official Agricultural Chemists, Bulletin 162, Bureau of Chemistry, find the melting point of aspirin to be from 130½° C. to 131° C.

In the past year we have examined eleven samples of this product, ten of which had a melting point of 135° C. while one we found to be 133° C. When it is remembered that aspirin will decompose before it melts, we have the probable explanation for the difference in the melting point. The length of time it is heated, etc., also probably affects the melting point. Emery and Wright recommend that the rate of heating be such as will give a rise of 1° C. per minute. The aspirin that would melt higher than 135° C. or lower than 130° C. we would, however, look upon with suspicion.

Test for Free Salicylic Acid.—Five Cc. of a 2 percent solution of aspirin in alcohol diluted with 20 Cc. of water should not be immediately colored violet upon the addition of one drop of ferric chloride test solution. *Caution*.—The solution should be prepared cold and must be fresh; not more than one drop of ferric chloride test solution should be used, as there is danger, due to the acidity of the latter, of breaking down the aspirin and getting violet color from the liberated salicylic acid.

Test for Free Acetic Acid.—Aspirin should be odorless and particularly have no odor of acetic acid, indicating absence of this acid.

Test for Hydrochloric Acid and Chlorides.—A five percent solution in alcohol mixed with a few drops of nitric acid should not be affected by the addition of silver nitrate test solution.

Test for Sulphuric Acid and Sulphates.—Five Cc. of five percent solution in alcohol diluted with 20 Cc. of water, and acidified with hydrochloric acid, should not be affected by the addition of barium chloride test solution.

A solution of the salt one in twenty should respond to the heavy metals test of the U.S.P. VIII.

Resinous Impurities.—An alcohol solution evaporated to dryness in a dish protected from the dust should give a perfectly white crystalline residue.

Phenol.—If one gramme of aspirin be dissolved in an excess of sodium carbonate test solution, the liquid agitated with an equal volume of ether, the ethereal solution allowed to evaporate spontaneously, the residue should be free from odor of phenol.

Readily Carbonizable Organic Impurities.—On treating about five grammes of aspirin in a test tube with 10 Cc. of concentrated sulphuric acid, no odor should be imparted to the latter.

Estimation of Acetyl-salicylic Acid.—May be estimated by boiling with sodium hydroxide and titrating excess of sodium hydrate, using phenolphthalein as indicator. One gramme of the aspirin is boiled with 15 Cc. of normal sodium hydrate for about five minutes, a few drops of phenolphthalein added; tenth-normal hydrochloric acid is run until the pink color is destroyed.

Allen's Commercial Analysis, volume 3, page 504, 4th edition, gives the following method for the estimation of acetyl-salicylic acid, which we have found to give excellent satisfaction in our laboratories. One gramme of the sample is weighed into a 200 Cc. flask, dissolved in a small quantity of alcohol, a drop of phenolphthalein solution added and titrated quickly as possible with tenth-normal potassium hydroxide solution, volume required being noted. To the liquid a volume of tenth-normal alkali, about five Cc. in excess of that already used, is added, the solution boiled for five minutes, an excess of alkali titrated with tenth-normal acid. The total volume of tenth-normal alkali required will be double that used in the cold neutralization, if the sample is free from salicylic or any other acid. If the sole impurity is salicylic acid, every 1/10 percent will decrease the total amount of alkali absorbed by one

gramme, 0.38 Cc. below 111.08 Cc.—the volume required by the pure acid. One Cc. of cold tenth-normal potassium hydroxide solution neutralizes 0.0180064 grammes, whilst the same volume of the boiling alkali reacts with 0.0090032 grammes of acetyl-salicylic acid. Since cold potassium hydroxide slowly hydrolyzes acetyl-salicylic acid, the cold titration must be effected quickly, or erroneous results will be obtained.

When combined with salts that interfere with the estimation by the above titration method, may be estimated colorimetrically, after it has been broken down, by the addition of ferric chloride and compared with definite amounts of aspirin treated in a similar manner; this may also be used to estimate the amount of salicylic acid present in aspirin, or to ascertain to what extent it has become broken down.

J. P. SNYDER.

ANALYTICAL LABORATORIES OF THE NORWICH PHARMACAL COMPANY.

INTERESTING ALKALOIDS AND GLUCOSIDES.

According to the *Pharmaceutical Journal* and *Pharmacist* of June 5th, investigation work on the drugs and poisonous plants of South Africa has been proceeding for some time at the Imperial Institute, and in the current number of the *Bulletin of the Imperial Institute* is published a summary of these investigations as far as completed.

The results obtained are interesting and valuable. Molteno disease, a cattle and horse disease prevalent in certain parts of the Union of South Africa, has been definitely traced to the presence of a poisonous alkaloid in a plant eaten by the animals. This plant is *Senecio latifolius*, a near relative of the common groundsel. "Cape slangkop," a plant belonging to the lily family, which causes cattle poisoning in other districts of the Union, contains a poisonous glucoside similar in action to that found in the common foxglove. Among other South African plants of which the properties are still being investigated at the Imperial Institute are the roots of the "Ntsema," which are said to be extensively used by the natives employed on the Witwaters Rand mines in the preparation of an intoxicating drink known as "kali."

GUM TRAGACANTH IN PERSIA.

According to a report by the United States Consul at Teheran, the various species of *Astragalus*, known in Persia as "kevin," from which gum tragacanth is obtained, grow on the mountain ranges which surround the Persian plain. The bushes producing the gum grow to a height of 2 feet. In the spring, when the sap rises, parts of the branches are cut away, thereby allowing the sap to flow out, which coagulates within a few hours on the surface of the stalk. The price of gum tragacanth has increased 5 to 10 percent since the outbreak of hostilities in Europe.

The principal Persian markets for gum tragacanth are Hamadan, Shiraz, Kerman, and Kermanshah. From 150 to 200 tons are exported annually from Hamadan alone. Before August 1st, 1914, half of this amount was shipped to Russia and the other half to America and the United Kingdom, but since that date the amount shipped to Russia has been reduced to one-fifth, the other four-fifths going to America and the United Kingdom.
