Papers Presented to Local Branches

ABSTRACT OF THE REPORT ON MEDICINAL PLANTS AND DRUGS AT THE LAST ANNUAL MEETING OF THE ASSOCIATION OF OFFICIAL AGRICULTURAL CHEMISTS.*

L. F. KEBLER, REFEREE.

During the past year the cooperative work on drug problems in conjunction with the Association of Official Agricultural Chemists has been very satisfactory. The number of cooperators taking part was unusually large and all manifested a spirit of interest in the work. The Referee's report was submitted under the following headings:

1. Methods of sampling.
2. Methods of analysis.
3. Inadequate standards.
4. Results.

It is well recognized that the procuring of representative samples for analytical work is the first important step in securing uniformity of chemical analyses. So long as we are not certain of obtaining samples which represent the total average of the material of a given consignment, we can never rely on the results directly setting forth the quality of the goods handled. In the taking of samples it is necessary to take into consideration the character of the goods to be sampled, the nature of the container, the probable climatic conditions obtaining, and the source of production. Experience covering a number of years shows the difficulty confronting the analyst, and in order to bring about uniform action and ultimately avoiding friction and reassaying, the referee recommended that a committee be appointed to take up the entire subject of drug sampling and report back to the Association at the next annual meeting. It is not unusual to meet with consignments containing hundreds of bales or bags or kegs or pockets or carboys or barrels, etc. The question naturally arising is how many packages shall be sampled in order to obtain material that will fairly represent the commodity under consideration. In the case of ergot, for example, it was found that one bag in ten may be found inferior and it sometimes happens that this one particular bag is selected for sample. The result is that the entire delivery is withheld. On the other hand if one of the other nine bags is sampled, the shipment is released with the result that the inferior package finds its way into the trade. It is exceedingly difficult to sample the bales of a large consignment so as to procure satisfactory results. It has been found that the outside of a bale, for example, will be perfectly satisfactory, whereas, the interior is of an inferior character. The number of bales to be examined is also a difficult matter to determine

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in every case. For example, one bale of belladonna root will show an alkaloidal content much below that prescribed by the standard, while many other bales of the same consignment comply with the standard. Under these conditions it has been found necessary at times to sample every bale, in an entire consignment in order to secure satisfactory results.

Similar questions were discussed in conjunction with gums, resins, oils, products solid at one temperature and liquid at another, semi-solids, balsams, etc.

Methods of Analysis: In order to arrive at a fair conclusion relative to an article, it is necessary to take into consideration all factors that may throw light upon the subject. The first point that naturally presents itself is the physical appearance of the commodity. If the article is not of normal appearance, suspicion is aroused immediately. The next two factors of great importance are odor and taste. Anyone familiar with these two factors of various crude drugs he is liable to meet is fortunate indeed. Much time may often be saved by submitting a given sample to microscopical examination before applying chemical methods. It is often necessary also to resort to mechanical means to determine the amount of foreign material that may be present in a given sample.

Inadequate Standards: The Pharmacopoeial standards for buchu leaves, for example, makes no provision whatever for the presence of any stems or other incidental foreign material which is liable to find its way into the drug at the time of collection. If such a standard were put into force and effect, the amount of this drug imported into the United States would be exceedingly small. In practice it has been found necessary to allow a certain amount of foreign material referred to above. What has been said in connection with buchu leaves also holds for many other leaves. Imitation balsam Peru complying with the test of the Pharmacopoeia in every detail has been met with. It is, however, not identical chemically with the natural product, neither has it been shown that its therapeutic properties are the same. The test prescribed by the Pharmacopœia for morphine sulphate permits the presence of a considerable quantity of codeine and other alkaloidal bodies derived from opium. In case the chemist is examining a sample of morphine sulphate according to the text prescribed by the Pharmacopœia and it complies in every respect with this test, he must of necessity report it as satisfactory. If this morphine sulphate containing a goodly proportion of codeine is now used in the manufacture of morphine sulphate tablets or other mixtures in which the morphine sulphate present is an important part, and the analyst discovers codeine, he immediately infers that the original material was contaminated with this alkaloid, or the product is not properly named, or may even be misbranded in view of the fact that the codeine is not declared, a condition which might cause some embarrassment.

The standards for the essential oils and the methods for arriving at same are very inadequate, as most analysts know. In fact, there is no difficulty whatever in manipulating some of the oils so as to comply with the standard prescribed in accordance with the methods detailed for arriving at same.

The standard for copaiba also is decidedly inadequate, it is believed, largely for the reason that we know so little about the actual composition of this commodity. In order to eliminate many of the uncertainties it will undoubtedly be

necessary to study the article from the source of production to the time of consumption.

Results: These can best be indicated by giving short resumés of the subjects considered which follow: H. H. Rusby, Associate Referee on macroscopic and microscopic study of plant drugs has been working on the subject of providing adequate descriptions of crude plant drugs not available at present. This will necessitate elaborating some of the standards for certain Pharmacopoeial drugs.

MEDICATED SOFT DRINKS.

G. W. HOOVER, ASSOCIATE REFEREE.

The work was confined to the determination of constituents (caffeine, cocaine, phosphoric acid) and the estimation of the total solids. The cooperative sample was prepared so as to represent as far as possible a number of preparations which have been found upon the market.

The results obtained by a majority of the chemists in the determination of caffeine were satisfactory. The figures show that if the method outlined is carefully followed, concordant and accurate results will be secured. The caffeine is obtained quite pure without subjecting it to a special method of purification.

The results for cocaine were slightly low. The quantity in the preparation, however, compared with caffeine, is quite small, and in view of the complex composition of the mixture, the results obtained in the estimation of cocaine were also satisfactory.

The method outlined for phosphoric acid is quite lengthy, but the results showed that if it is strictly followed, an accurate determination of this constituent can be made.

The results of the method for the determination of total solids showed too wide a variation. It was found that more concordant results were obtained by using a comparatively small quantity of the sample (2 to 4 grams) than by using a larger quantity, and it is evident that further work upon the determination of total solids is necessary.

HEADACHE MIXTURES.

W. O. EMERY, ASSOCIATE REFEREE.

In the past the cooperative work has had to do with mixtures of the referee's compounding, while that of the year just completed involved commercial products obtained on the market. The preparations were in tablet form. Twenty tablets together with the necessary directions for procedure were furnished each of the dozen co-workers. One mixture sent out contained as active ingredients caffeine, and acetphenetidin; another, codeine, acetanilide and sodium salicylate; and a third, codeine sulphate, antipyrine and acetphenetidin.

In general, the results may be considered very satisfactory in view of the inherent difficulties peculiar to certain preparations involved; more particularly, however, for the reason that probably one-half of the collaborators had not had any previous experience with such work, all of which indicates that the methods submitted are correct in principle and need only to be varied in detail to meet the problems arising from special combinations.

A method was devised in connection with the examination of mixtures containing caffeine, acetanilide, quinine and morphine. The separation is based on the solubility of caffeine and acetanilide in chloroform, while the sulphates of quinine and morphine are insoluble in this reagent. The alkaloids were separated from each other by virtue of the insolubility of sodium morphinate in the aforesaid solvent. The morphine itself being finally extracted as such with chloroform (carrying a little alcohol) from an aqueous solution containing common salt in excess together with a little ammonium salt.

W. O. Emery and C. D. Wright undertook a study of aspirin tablets and capsules, more especially melting temperature alone and in admixture with salicylic acid in various proportions, and finally the acid values of these compounds.

C. C. LeFebvre investigated the method of determining salol alone as well as in admixture with acetphenetidin, having already succeeded in estimating salol both in separate form and in original tablets by hydrolyzing into phenol and salicylic acid and subsequently titration with a standard bromine solution.

COOPERATIVE WORK ON THE DETERMINATION OF CAMPHOR.

E. K. NELSON.

A sample of Spirit of Camphor, prepared carefully according to the Pharmacopoeia was submitted to twenty-three analysts for the determination of camphor by the hydroxylamine titration method as outlined in Circular No. 77 of the Bureau of Chemistry. The results reported by nineteen analysts varied from 8.33% to 9.72%, while four analysts found slightly more camphor than was actually present.

The average of all results reported was 9.02%, or a deficiency of nearly 10% figured on the camphor actually present. The consensus of opinion as expressed by the various analysts was that the conversion of camphor into oxim was not complete. The method can not, therefore, be recommended for exact work.

THE DETERMINATION OF SMALL QUANTITIES OF PEPSIN IN LIQUIDS.

V. K. CHESTNUT.

The method used in this work was essentially the Jacoby procedure as modified bySolm. A 0.4 per cent. solution of U. S. P. pepsin in N/10 hydrochloric acid previously saturated with chloroform was sent out together with some standard pepsin and ricin. The sample was analyzed by seven cooperators. The results reported varied widely. One analyst reported 1 per cent., but the others found between 0.09 and 0.38 per cent. The particularly interesting feature of the results was that the reports seemed to indicate a somewhat uniformly progressive decomposition of the pepsin due perhaps partly to the summer temperature and agitation to which they were subjected or to the action of the chloroform added to the hydrochloric acid to conserve the pepsin against the action of molds. The highest percentage found was obtained at Washington in a sample kept in cold storage and analyzed three days after it was made up. The same sample yielded only 0.2 per cent. 40 days later, and another held at room temperature during the 40 days gave only 0.1 per cent.

ESTIMATING NITROGLYCERIN IN TABLETS.

A. G. MURRAY.

Cooperative work on nitroglycerin tablets was carried out on two samples. Nineteen collaborators reported. Considering the rather complicated nature of the methods, the minute quantity of nitroglycerin to be determined, and the lack of experience with the methods of many of the collaborators, the results were as good as could be expected. The completeness of the extraction of nitroglycerin from the tablets should be investigated.

A STUDY OF THE LEAD NUMBER OF ASAFOETIDA AND ALLIED PRODUCTS.

E. C. MERRILL.

This is a method of measuring the lead precipitate of asafoetida and various other similar products by precipitation of a gram sample of the ether purified resin (dried five hours at 110° C.) by means of a 5% lead acetate solution in 80% alcohol. The uncombined lead is determined by filtering off an aliquot portion and determining the lead as sulphate. By carrying a control test the amount of lead combined may be calculated from the difference of the two, and the lead number expressed in terms of milligrams of metallic lead per gram of sample.

The following results have been obtained:

Asafoetida 222, galbanum 4, ammoniacum 75, olibanum none, guaiac 171, myrrh 7, colophony 142, bedllium 55, sandarac 251, mastic 34, gamboge 9, dragon's blood 0, euphobium 34, "pepper asafoetida" 82.

This method gives results which may be checked by independent workers although the value is not absolute on account of incomplete drying of the ether purified resin. It is however sufficient to give comparative results.

COOPERATIVE RESULTS ON MORPHINE ESTIMATION.

H. E. BUCHBINDER.

The method studied was that proposed by Eaton. The main features of the method for opium are as follows:

The opium is digested in lime water, the lime water is filtered and an aliquot taken. The latter is shaken out repeatedly with chloroform to remove other alkaloids, then ammonium chloride is added and the morphine is shaken out with a mixture of chloroform and alcohol. The latter is evaporated and the residue titrated with standard acid and standard alkali.

The methods for paregoric and syrup are adaptations of the opium method.

The results of the collaborators showed that in case of powdered opium the conditions prescribed do not insure the complete exhaustion of the powder, also that it is practically impossible to get rid of the other alkaloids by direct extractions. The results on paregoric were decidedly better than those on opium, but were not altogether satisfactory.

Gave the results of a study of a number of topics having a bearing on certain analytical methods for morphine.

1. *Does chloroform take up morphine from an alkaline (fixed alkali) solu-*

tion? It was found that with a certain excess of alkali the amount taken up is negligible.

2. *Chloroform plus alcohol as a solvent for morphine.* In this connection the distribution of alcohol between chloroform and water, as well as solubility of morphine in chloroformic alcohol and aqueous alcohol, were studied.

3. *Chloroform alone as an extracting solvent.* Conditions were found under which small quantities of chloroform can be used with great convenience to extract morphine from an aqueous solution. This is made possible by the conversion of the morphine into a form ten times more soluble than the ordinary "crystalline" variety.

4. *The Eaton methods.* The chief defect is the practical impossibility of removing the other alkaloids from the lime water solution. A "negative" test is misleading.

5. *An error of the U. S. P. method.* The amount of morphine remaining in the mother liquor was found to be about 140 mgms.

6. *New methods for opium and opiates.* The salient features are: First, the use of chloroform alone as an extracting solvent for morphine; second, the use of barium salts as precipitants of resinous impurities, thus entirely overcoming the difficulty of emulsions.

The following is a brief outline of the proposed method for powdered opium.

The initial extraction of the powder is effected by digestion with hot water, followed by the addition of 10% sodium hydroxid and shaking during a short interval. The solution is saturated with salt, diluted with saturated salt solution, and after the addition of barium chlorid, is made up to volume with saturated salt solution. After filtration an aliquot is taken. The latter is acidified with concentrated hydrochloric acid and then rendered ammoniacal with concentrated ammonia, the quantities of the acid and the ammonia being carefully regulated so as to secure certain definite concentrations of free ammonia and ammonium salts. After the addition of some alcohol, the morphine, accompanied by a certain amount of other alkaloids, is extracted with chloroform. A few extractions with very small quantities of a saturated salt solution containing about 2% of sodium hydroxid, take out all the morphine from the chloroform extract. The almost negligible amount of other alkaloids carried by the alkaline-salt extractions is removed by means of one or more shake-outs with chloroform. The morphine is then re-extracted with chloroform under conditions similar to those in the first extraction with chloroform. After the evaporation of the chloroform, the residue is titrated by means of standard acid and alkali. With experience the entire analysis can be completed within 2 1/2 hours.

Methods are also offered for laudanum, paregoric, etc. Those are adaptations of the basic method—that for opium.

A COMPARISON OF VALUES OBTAINED FOR THE REFRACTIVE INDICES OF AQUEOUS SOLUTIONS OF ETHYL AND METHYL ALCOHOLS.

B. H. ST. JOHN.

This paper embodies the comparison of the values obtained by different investigators for the refractive indices of the aqueous solutions of ethyl and

methyl alcohols reduced to the same temperature by means of the temperature coefficients given by Doroshevski. The values compared are those of Deville, Wagner, Leach and Lythgoe, Doroshevski, and Andrews for ethyl achohol; and of Drude, Wagner, Leach and Lythgoe, and Doroshevski for methyl alcohol.

HABIT-FORMING DRUGS.*

S. L. HILTON.

To all of us this subject is more or less familiar and generally speaking we as pharmacists have a very clear understanding as to what are or what are not habit-forming drugs. However, many drugs that were considered a few years ago as harmless have been proven harmful and habit-forming, this is probably best illustrated by one of the so-called derivatives of morphine, heroin or di-acetyl morphine.

There is not today a morphine habitue who will not as readily use heroin as they formerly used morphine. The sale of heroin or di-acetyl morphine or its tablets, has increased tremendously, not only with the drug trade, but large quantities of the drug have been disposed of by peddlers to habitues, so that those having the enforcement of drug laws have been compelled to use every means at their command to circumvent this traffic.

At the outset, and after this condition became known, it seemed almost impossible with the present laws to reach the real offenders, however, after consultation with many who were in a position to advise, and after much deliberation a decision was reached to bring a case in court with the hopes that something might be done. This was tried, with the result that the court held that heroin came under the provisions of Sec. 11, of the "Act to regulate the practice of pharmacy and the sale of poisons," that heroin was a salt of morphine, consequently the law had been violated, as the sale had not been made on prescription, and imposed a moderate penalty. Since then several more cases have been tried with like results.

While this is a decision of the lower or Police Court, no appeal in any case having been taken, it consequently stands as to settling the status of heroin, in the District of Columbia, unless or until in some future case brought it is carried to the Appellate Court of this District. It is not for me to predict what a higher court might or might not decide if such a case is brought, but it would seem that, using the rule of reason as defined by the U. S. Supreme Court, and taking into consideration the proper protection of the public health, coupled with the fact that heroin is a product of morphine, and by many authorities considered the di-aceate of morphine, it is reasonable to expect that the higher court would so construe the law as to include heroin or di-acetyl morphine as a salt of morphine, thereby approving the decision of the Police Court.

With the decision of the Police Court and unless it is reversed by a higher court all sales of heroin or its salts, in the District of Columbia, can only be

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