IMPROVEMENTS IN PROCESSES FOR THE IDENTIFICATION AND DETERMINATION OF ALKALOIDS.

(Progress of a Decade.)

BY L. E. WARREN, H. R. WATKINS AND G. L. KEENAN.

Because of their importance in medicine, alkaloids and alkaloid-bearing drugs are of great interest to the chemist. Methods for the assay of drugs have been studied for more than 125 years, and since the U. S. Pharmacopœia first introduced drug assays, about 50 years ago, the recorded researches in this field have reached an enormous volume. During the past decade the studies having a direct bearing on the detection and determination of alkaloids are very numerous. In a review suitable for this symposium it is manifestly impossible to even mention all of the publications on the subject. Therefore, only those contributions are mentioned which report advances judged to be of outstanding importance. So far as practicable the discussion has been limited to alkaloids employed in medicine. The topic is considered under several sub-headings, such as methods of extraction, solvents, precipitants, gravimetric methods, titrimetric procedures, color reactions, microscopical tests, etc.

In 1921 Herzig[1] undertook to assemble the numerous methods that had been suggested for the determination of alkaloidal constituents in crude drugs and their products. Gravimetric, volumetric, colorimetric and polariscopic methods are critically discussed.

METHODS OF EXTRACTION.

Many forms of automatic extraction apparatus have been devised to replace tedious hand operations in analytical chemical methods. Their application to the extraction of alkaloids from solutions by immiscible solvents has received considerable attention during the past decade. Some of the most important contributions to the estimation of alkaloids, from the standpoint of their ultimate effects on analytical processes, are the improvements in automatic extraction apparatus reported by Palkin, Murray and Watkins.[2,3] Two types of extractors were used (*a*) for solvents lighter, and (*b*) for solvents heavier than water.

The efficacy of the inner tube for solvents of lighter gravity depends very essentially upon the diameter of the holes and the flow of solvent through them. Twelve holes of a diameter of 0.31 mm., instead of 16 as originally suggested, are recommended.

The automatic extractors for aqueous liquids were applied to such preparations as fluidextracts, tinctures, elixirs, syrups and solutions of tablets of alkaloid salts. The application of the automatic extractors to galenical preparations of nux vomica, belladonna and stramonium, gave very satisfactory results and did away with the tiresome methods using the hand-shaken separators. In the case of fluidextract of ipecac, higher results were obtained than by the U. S. P. method for this article.

A third type of extractor utilizing the principal parts of the types described in the original papers, such as boiling flask, condenser and jacket but equipped with different inner parts is employed in extracting powdered materials such as hyoscyamus, ipecac, belladonna, nux vomica, etc. The flow of solvent is upward through the powder.

The effectiveness of the apparatus and the method of treatment were thoroughly demonstrated in a large number of assays of hyoscyamus; the quantity of alkaloid extracted amounting, in some cases to three times that obtained by the method of the U. S. Pharmacopœia. The extractor was used successfully for such crude drugs as hyoscyamus, belladonna, ipecac, stramonium and nux vomica. In addition to the apparatus described above several devices have been suggested for the extraction of the active principles from drugs.[4]

---

[1] *Arch. Pharm.*, 259 (1921), 249, 308.

[2] *Ind. Eng. Chem.*, 17 (1925), 612. [3] *Ibid.*, 19 (1927), 535.

[4] *Chem. Drug.*, 111 (1929), 230.

SOLVENTS.

In the assay of belladonna leaves Caines and Evers[1] found that a mixture of four volumes of ether and one volume of chloroform gave much less troublesome emulsions than the solvent recommended by the U. S. P. X, *i. e.*, three volumes of ether and one volume of chloroform.

Beal and Hamilton,[2] in continuing their studies on the quantitative determination of alkaloids by immiscible solvents, studied caffeine, morphine, quinine and strychnine. They concluded that the use of lead acetate as a clarifier has no harmful effect upon the subsequent extraction of the alkaloids. The addition of sodium chloride to such extracts, after clarification, increases the amount of alkaloid that may be extracted by a single shake out. The assay of nux vomica was greatly facilitated by extracting the ground drug with weak acid, clarifying the extract with lead acetate, making the solution alkaline and shaking out immediately with the immiscible solvent.

At ordinary temperature morphine requires about 1530 parts of chloroform for solution. Under certain conditions, however, chloroform has been found to be a good solvent for removing the alkaloid from solutions. It has been known for some time that if chloroform be diluted with from $^1/_4$ to $^1/_9$ of its volume of alcohol the mixture will dissolve morphine quite readily, particularly if the aqueous solutions containing the alkaloid be saturated with salt. Early in the decade Glycart and his collaborators in the A. O. A. C.[2a] worked out details for the satisfactory analysis of morphine tablets, using a mixture of 9 volumes of chloroform and 1 volume of alcohol as immiscible solvent in presence of sodium chloride. Palkin, Murray and Watkins[3] found that morphine could be extracted readily from aqueous solutions by chloroform by the use of automatic extraction apparatus.

BENZENE AS IMMISCIBLE SOLVENT.

The use of benzene as an immiscible solvent for the extraction of alkaloids is not new, although its employment for that purpose has never become general. During the past decade several contributions have appeared which indicate that this solvent might be employed with advantage to a much greater extent than it now is in the extraction of alkaloids. Deane and Edmonton[3] employed benzene instead of chloroform in extracting the crude alkaloids from the extract and fluidextract of nux vomica. Chloroform was used for the final extraction of the alkaloids after acid purification. They stated that higher results were obtained with benzene as initial solvent than with chloroform, due to the prevention of losses by the formation of emulsions. The results were the same regardless of whether sodium carbonate or sodium hydroxide were used to liberate the alkaloids.

In the assay of fluidextract and tincture of nux vomica Palkin and Watkins[4] observed that the use of benzene as a solvent gave alkaloidal residues containing less coloring matter than were obtained by the employment of chloroform. This is a distinct advantage particularly if the residues are to be titrated. As a rule alkaloids are much less soluble in benzene than in chloroform but this handicap is not serious if automatic extraction apparatus be employed.

DECOMPOSITION OF ALKALOIDS BY CHLOROFORM.

It has been suspected for some time[5] that certain alkaloids, particularly the more strongly basic ones, when evaporated in chloroformic solution, have a tendency to decompose the solvent with the formation of a hydrochloride of the alkaloid. This phenomenon results in higher values by gravimetric processes and in lower findings by titration. The errors due to this decomposition, however, are usually small.

Rosin[6] has studied this phenomenon and he concluded that strychnine is among the most troublesome alkaloids in this respect. He believes that during the process of evaporation, traces

[1] *Pharm. J.*, 117 (1926), 179.

[2] JOUR. A. PH. A., 9 (1920), 9.

[2a] *J. Assoc. Official Agr. Chem.*, 5 (1921), 150.

[3] *Pharm. J.*, 113 (1924), 96, 133.

[4] JOUR. A. PH. A., 13 (1924), 691. *Ind. Eng. Chem.*, 17 (1925), 612.

[5] Simmer, *Arch. Pharm.*, 244 (1906), 672.

[6] Private Communication to the authors.

of the solvent are retained by the alkaloid. In heating the residue at 100° C. to expel the solvent, interaction takes place between the alkaloid and the chloroform, with the resultant formation of an alkaloidal hydrochloride. The remedy lies in the selection of some other solvent for the extraction of the alkaloids or, if the alkaloid is to be titrated, in adding a measured excess of standardized acid to the partially evaporated chloroformic solution and continuing the evaporation until the solvent has been expelled. The titration may then be completed.

Watkins and Palkin[1] found that much of the chloroform on the market is unsuitable for use in alkaloidal assays, although it complies with the U. S. P. tests for purity. Incomplete recovery of known amounts of alkaloid results from the use of such chloroform. They believe that the fault is due largely to partial neutralization of the alkaloid by the solvent during the process of assay. In most instances the solvent could be purified sufficiently by refluxing it over a strongly basic alkaloid, such as brucine. Apparently the only method at present available by which a specimen of chloroform may be ascertained to be sufficiently pure for alkaloidal assays is to try it on a given weight of a known alkaloid. It is preferable to employ benzene as solvent in place of chloroform where applicable. Watkins and Palkin found that benzene is suitable for atropine, brucine, codeine, quinine and strychnine and for galenicals containing them. It is not satisfactory for morphine.

VOLUMETRIC PROCEDURES.

Rasmussen and Christensen[2] recommended the use of 0.05 *N* sodium borate as the most satisfactory alkali to be used for the back titrations of acid in alkaloidal assays.

Ionescu and Spirescu[3] have developed a new volumetric procedure for the determination of alkaloids which is based on the titration of the mercuric ion with chlorine. The method had previously been used for the determination of acetone.[4] The alkaloidal material is precipitated by an acid solution of mercuric potassium iodide, the precipitate is dissolved in a mixture of nitric acid and sulphuric acid, the excess of nitric acid is destroyed by potassium permanganate, and the mercury determined by standardized sodium chloride, using sodium nitroprusside as indicator. The sodium chloride factor for each alkaloid must be known or previously determined.

ELECTROMETRIC TITRATIONS.

In the last decade a great deal of work has been done in determining the p_H values of solutions of alkaloidal salts; also the p_H ranges of many indicators have been ascertained. As a result, a more rational choice of indicators for alkaloidal titrations has been made possible. Some workers have used the hydrogen electrode; others have employed the quinhydrone electrode; still others have used a platinum electrode.

Wales[5] determined the p_H values for over 30 alkaloids, using the quinhydrone electrode, and has suggested the proper indicator to use in the titration of each, except for two which could not be titrated. Methyl red was found to be a suitable indicator for 18 of the alkaloids tested. Other indicators suitable for certain alkaloids were propyl red, bromocresol purple and bromophenol blue.

The chief advantages claimed for the electrometric titration over the older methods are (*a*) greater accuracy due to a more definite determination of the end-point, (*b*) ability to make titrations without regard to the color of the solution. This permits of titrations of crude extracts of alkaloids, thus eliminating the necessity for time-consuming purification processes.

Sterkin and Helfgat[6] have described a new reagent for the nephelometric detection of minute amounts of quinine. It is composed of equal portions of 0.12% of sodium arsenate, 2% ammonium molybdate and 2% of hydrochloric acid. It is claimed to be the most sensitive known reagent for quinine, 1 part in 2,000,000 being detectable. The reagent is less sensitive for other alkaloids, such as caffeine, apomorphine, morphine and plasmochine.

---

[1] *Ind. Eng. Chem.*, 18 (1926), 867.
[2] *Dansk Tids. Farm.*, 1 (1926), 65.
[3] *Bull. soc. chim. Romania*, 5 (1923), 74.
[4] *Bull. soc. chim.*, 33 (1923), 110.
[5] *Ind. Eng. Chem.*, 18 (1926), 390.
[6] *Biochem. Z.*, 207 (1929), 8.

SOLUBILITIES.

Zeehuisen[1a] has tabulated the physical properties of about 40 alkaloids. He includes the formula molecular weight, crystalline state, melting point, solubilities, etc. This information should prove of considerable value to analysts.

APOMORPHINE.

The determination of apomorphine offers considerable difficulty because the substance is prone to decompose under the conditions of the usual processes of analysis. Recognizing the desirability of having an accurate method for the determination of apomorphine hydrochloride, Eaton and his collaborators in the A. O. A. C.[2] studied methods for the determination of this substance in tablets. The method tentatively adopted by the Association consists in liberating the alkaloid from its salts by a saturated solution of sodium bicarbonate, extracting the liberated alkaloid with ether, washing the ethereal solution of the alkaloid with water, adding a measured excess of standardized acid, evaporating the ether and titrating the excess acid with standardized alkali, using methyl red as indicator. Obviously it is necessary to employ ether that is free from peroxides for this assay.

COCAINE.

Owing to the fact that cocaine is very unstable when subjected to heat or to the action of acids or alkalies, the usual analytical processes for alkaloids are not applicable to preparations containing this alkaloid. Eaton and his collaborators[3] in the Association of Official Agricultural Chemists, worked out a method by which the alkaloid was liberated by sodium bicarbonate, the liberated alkaloid removed by shaking with petroleum benzin, the solvent washed with water and afterward shaken with a measured excess of standardized acid. The acid solution was removed and titrated with standardized alkali, methyl red being used as indicator. These authors also developed a method by which the cocaine was hydrolyzed and the benzoic acid isolated and determined. The last named method was not as satisfactory as the first. Another method used by the A. O. A. C.[4] consisted in liberating the alkaloid with ammonia and shaking out the alkaloid with peroxide-free ether, after which the base was titrated.

EPHEDRA.

Ephedra has been known in Chinese medicine since very early times. Its principal alkaloid, ephedrine, was introduced into occidental medicine only within the past decade. A number of contributions on the assay of ephedra and its preparations have appeared. In general the U. S. P. X process for the assay of belladonna leaves with slight modification has been found satisfactory, certain precautions being taken to prevent losses of the alkaloids by volatilization or oxidation. The collaborators of the Association of Official Agricultural Chemists have elaborated a method[5] for the assay of ephedra, by which the alkaloids, after being liberated by a mixture of sodium carbonate and ammonia water, are taken up with a mixture of chloroform and ether. After purification by the acid shake-out process, the alkaloids are liberated by the dual alkali above mentioned and extracted with ether. The solution is evaporated somewhat and a measured excess of standardized acid added. After further evaporation to remove the remainder of the solvent, the excess acid is titrated with standardized alkali, bromothymol blue being used as indicator.

The alkaloids of ephedra are chiefly ephedrine and pseudo ephedrine, the relative proportions in which they occur being about as 4 to 1. Chou[6] observed that pseudoephedrine oxalate is soluble in water while ephedrine oxalate is very insoluble. This property may be used to separate the two alkaloids. Reed and Feng[7] found that pseudo-ephedrine hydrochloride is

[1a] *Arch. exptl. Path. Pharmakol.*, 86 (1920), 343.
[2] *J. Assoc. Official Agr. Chem.*, 8 (1925), 572. *Ibid.*, 9 (1926), 323. *Ibid.*, 10 (1927), 379.
[3] *Ibid.*, 10 (1927), 347.
[4] *Ibid.*, 11 (1928), 49, 328.
[5] *J. Assoc. Agr. Chem.*, 12 (1929), 290.
[6] *J. Biol. Chem.*, 70 (1926), 109.
[7] *Chi. Jour. Physiol.*, 1 (1927), 297.

about 53 times more soluble in chloroform than ephedrine hydrochloride. An approximate separation of the two alkaloids may be made by an application of this phenomenon.

ERGOT.

The pharmacodynamic activity of ergot lies in two groups of compounds, *viz.*, specific alkaloids and non-specific amino-bases. The desirable therapeutic properties are found in two of the four alkaloids, the other two being inert. The non-specific amines, while of no therapeutic activity are not devoid of physiological power. Their presence in ergot preparations is, therefore undesirable, because of this influence on certain types of bio-assays. A chemical determination of the alkaloids in ergot is of very little value in judging the therapeutic usefulness of the drug, because of the presence of variable amounts of the weak or relatively inactive alkaloids. Some form of bio-assay is necessary.

Thompson[1] has developed methods for separating the non-specific amines from ergot and its preparations after which the specific alkaloids may be obtained in a state of relative purity suitable for bio-assays. He has also worked out a process for the preparation of purified fluid-extract of ergot. The preparation owes its activity to the specific alkaloids. The defatted drug is percolated with weak sodium bicarbonate solution to remove the non-specific amines. The drug is then percolated with an acid, hydroalcoholic menstruum, which removes the specific alkaloids. The activity of this percolate is then determined by biological tests, preferably by the isolated rabbit-uterus procedure.

MYDRIATIC ALKALOIDS.

Several observers have noted that certain mydriatic alkaloids, such as atropine and hyoscyamine are prone to decompose during the analytical manipulations with resultant findings that are low.[2,3,4,5] Gadamer[6] showed that water has a marked hydrolytic effect on these alkaloids. Self[7] believed that the losses were due to the liberation of ammonia from its salts by the alkaloids with consequent lowering of their titrimetric values. Dott[5] concluded that the hydrolysis was brought about by the alkalies used to liberate the alkaloids. Jones[5] noted in 1923 that if a chloroformic solution of the alkaloids of belladonna (as obtained in assay processes) be evaporated by the use of heat some decomposition of the alkaloids will occur owing to the deleterious effect of the moisture in the chloroform. This phenomenon was investigated by Palkin and Watkins.[6] They found that if about 50 cc. of a chloroformic solution of atropine or hyoscyamine, containing a little water and ammonia, were evaporated to a volume of from 5 to 10 cc. all of the ammonia is dissipated. If a measured excess of standardized acid be then added and the remainder of the chloroform then evaporated no decomposition of the alkaloid resulted. The excess acid in the cooled solution may then be titrated. These authors also found some evidence to indicate that if half a volume of neutral, absolute alcohol be added to the concentrated chloroformic solution the evaporation may be continued until dryness is reached without decomposing the alkaloids. This last observation requires confirmation. The precautions advocated by Palkin and Watkins would appear to be of considerable importance in the assay of preparations containing mydriatic alkaloids.

OPIUM.

Since the time of the Egyptians[8] opium has been considered one of the most important drugs. It is official in most pharmacopœias and many of them describe its galenical preparations or alkaloidal derivatives. The most important alkaloid in opium is morphine and most assay methods for opium are directed solely toward the determination of this alkaloid. A rapid and accurate method for the assay of opium has been the desire of chemists for more than one hundred

[1] JOUR. A. PH. A., 19 (1930), 705.
[2] Will and Bredig, *Ber.*, 21 (1888), 2797.
[3] *Arch. Pharm.*, 239 (1901), 294.
[4] *Pharm. Jour.*, 94 (1915), 521.
[5] *Ibid.*, 107 (1921), 286.
[6] Year Book Pharm., 60 (1923), 702.
[7] JOUR. A. PH. A., 16 (1927), 21.
[8] Wooton, "Chronicles of Pharmacy," 1 (1915), 34, *et seq.*

years and no other drug has received so much analytical attention in research directions as this. A great many papers and at least two inaugural dissertations concerning the assay of opium have appeared during the last decade.

Undoubtedly the most important contribution to the subject is an inaugural dissertation by Hollman.[1]

In 1920 Jermstad[2] reported an exhaustive study of numerous methods for the assay of opium. He considered the procedure under 6 classes. He found that all of the official lime methods (U. S. P. IX, B. P. 1914, Codex (1908), Japan, III, Netherlands IV, and Spain) gave impure morphine and the results were generally too high. If the morphine be freed from narcotine and calcium meconate by means of alcohol the results agree with the Helfenberger (water extraction) method.[3] Of the unofficial lime extraction methods tested by Jermstad, only that of Beckurts is usable. He could find but very little difference between methyl red and iodeosin as indicators. As a result of his observations, Jermstad devised and recommended a modification of Helfenberger's method in which lime is not used. Jermstad's method was not adopted by the U. S. P. X.

In consulting with analysts we found that almost the only criticism offered of the U. S. P. X assay process for opium (other than its length) is that too little distilled water is directed to be used in extracting the drug. We are informed that the Import Office of the Treasury Department of the Government uses the U. S. P. X method of assay and that this Office has no criticism of the method to offer.

MICROSCOPICAL TESTS.

In the microscopical identification of the alkaloids, two methods may be employed. The most familiar one, the microchemical, relies upon the formation of a characteristic crystalline precipitate which is produced upon the application of a reagent. A chemical reaction takes place with the resultant formation of crystals or groupings of crystals, the individual crystals or aggregates of these being so characteristic that they are useful for identification purposes. Another method which has been more commonly used during the past decade for the identification of the alkaloids is the immersion method which requires that the alkaloid or its salt be crystalline. In contradistinction to the microchemical method, no reaction takes place between the alkaloid (or salt) and reagent to produce a crystalline precipitate but the crystalline material is mounted in a suitable menstruum (usually oily in nature), and certain physical characteristics are observed and measured with the microscope. This method will be discussed more in detail subsequently. Within the limited space assigned to this discussion, it will be possible to review only some of the outstanding developments in the microscopical identification of the alkaloids which have taken place in the past ten years. The achievements in the strictly microchemical field first will be considered.

In the early part of the past decennium, Stephenson's[4] work on the microchemistry of the alkaloids appeared. This is probably one of the most exhaustive compilations of tests in English. It contains a table of reactions of fifty-one alkaloids with thirty-five reagents and is illustrated with one hundred sixty-two photomicrographs. Somewhat later (1922) the work of Nelson and Leonard[5] on the picrates appeared. They worked out a convenient reference chart for quickly placing the precipitates into crystal groups for the purpose of determining from the "habit" of the crystals what base might be present.

---

[1] Dissertation, Amsterdam (1926); *Pharm. Weekblad*, 63 (1926), 1337, 1370, 1393.

[2] Dissertation, Basel (1920); *Schweiz. Apoth. Ztg.*, 58 (1920), 277, 289, 301, 421, 462; *Repert. Pharm.*, 32 (1920), 257.

[3] Helfenberger, *Annalen* (1897), 188.

[4] "Some Microchemical Tests for Alkaloids" (1921).

[5] *J. Am. Chem. Soc.*, 44 (1922), 369.

The methods followed in the studies of Heiduschka and Meisner[1] were chiefly concerned with the extraction and sublimation of the alkaloids and their subsequent identification by many well-known microchemical tests, such as those given in the texts of Tunmann,[2] Behrens[3] and others. Sublimates of the following alkaloids and salts were studied: caffeine, theobromine, strychnine, cinchonine, morphine, codeine, apomorphine hydrochloride, thebaine, narcotine, quinidine, quinine, atropine, cocaine, brucine, scopolamine hydrobromide, aconitine, narceine, colchicine and veratrine.

For the identification of procaine in concentrations of five per cent, Deniges[4] recommended a five per cent solution of $NaClO_4$, a drop of which is added to the sample to be tested. In the early part of the reaction, spheroidal particles appear, but on stirring, rod-shaped crystals of procaine perchlorate will gradually form (illustration shown in original paper). When the free base is at hand, it is preferable to dissolve it in five to ten per cent acetic acid preliminary to making the final tests.

In 1923 Cole[5] considered the use of potassium ferrocyanide as a reagent for alkaloids. Previous to this time this reagent had been used, but a complete list of the alkaloids yielding crystalline precipitates with it had not been made.

The work of Maplethorpe and Evers[6] in 1925 described the picrates of the opium alkaloids, these being crystallized from various percentages of alcohol (methylalcohol in the case of morphine picrate).

In 1925 (and later in 1928), Cumming and Brown made a very extensive and systematic study of the hydroferro- and hydroferricyanides of a number of alkaloids. In the first section of the work,[7] the hydroferrocyanides and hydroferricyanides of the following alkaloids were prepared: cinchonine, quinine, cocaine, narcotine, brucine and strychnine.

The second part[8] of the work applies the same technique to the following alkaloids: sparteine, cinchonidine, hydrastine, nicotine, pilocarpine, piperine, narcotine, ecgonine, codeine and morphine.

Van Urk[9] in 1927 obtained crystalline precipitates with morphine when tested with $HgCl_2$, IKI, $KBiL_4$ and CsCdI. Codeine gave a characteristic precipitate with picrolonic acid and also with KSCN and $PtCl_4$ in addition to the reagents used for morphine.

Some attention was given by Beckman[10] to the identification by sublimation, color tests, and crystallization of eighteen alkaloids and substances containing them.

More recently Glycart[11] and his collaborators have been testing out the microchemical methods for various alkaloids in connection with the work of the Association of Official Agricultural Chemists. It is the intention of this collaborative work to ascertain how reliable these various tests are in the hands of different workers, and the effect of possible variations in technique on the resultant crystalline formations. Cocaine, codeine, heroin, morphine, strychnine, atropine, brucine, caffeine, pilocarpine, and the principal alkaloids of cinchona have been studied.

OPTICAL-CRYSTALLOGRAPHIC STUDIES.

The optical immersion method, as already indicated in the early part of this paper, is concerned with the determination of certain physical constants on crystalline material immersed in liquids of known refractive index. Among other constants, which may be measured, the refractive indices of a crystalline substance are the most important and diagnostic for deter-

---

[1] *Archiv der Pharmazie*, 261 (1923), 102; 265 (1927), 455.

[2] "Pflanzenmikrochemie" (1913).

[3] "Anleitung z. Mikrochem. Anal." (1895–1907).

[4] *Bull. Soc. Pharm., Bordeaux*, 62 (1924), 119.

[5] *Philippine J. Sci.*, 23 (1923), 97.

[6] *Pharm. J. and Pharm.*, 115 (1925), 137, 178.

[7] *J. Soc. Chem. Ind.*, 44 (1925), 110T; 47 (1928), 84T.

[8] *Pharm. Weekbl.*, 63 (1926), 560.

[9] *Ibid.*, 64 (1927), 371.

[10] *Pharm. Ztg.*, 73 (1928), 1165. *Ibid.*, 74 (1929), 28.

[11] *J. Assoc. Official Agr. Chem.*, 10 (1927), 370; 11 (1928), 353; 12 (1929), 282; 13 (1930), 315.

minative purposes. In order to determine these various optical properties it is necessary to make use of a polarizing microscope, equipped with an analyzing and polarizing nicol and the other accessories with which such an instrument is usually provided. The material to be studied is finely powdered and a small amount immersed in a liquid of known refractive index, this liquid usually being oily in nature. By repeated trials in different liquids it is possible to establish definite refractive index values which are very useful in identifying an alkaloid or its salt. Most of the crystalline alkaloids will have three significant refractive indices. However, as Benedict[1] has already pointed out, partial optical data are often very important, and, although at most only two indices of refraction may be determined on some substances, these are very useful and suffice for identification purposes. Of course, for a complete optical description of a substance for the first time, it is essential that all the optical data which it is possible to obtain be recorded.

The application of such a method makes its usefulness practicallly unlimited. Petrographers have made wide use of it for the identification of natural minerals and Wright[2] in 1916 called attention to its possibilities as an aid in analytical work, and was one of the first to indicate its application to the study of alkaloids. In 1918 Wherry[3] described the method in detail, especially with reference to the microscopical identification of alkaloids. Minute directions are given for the study of the material first in ordinary light, giving attention to the color or hue of the substance, its crystal habit, such as the geometrical form or outline of the crystals, a determination of the interfacial angles, and the refractive indices, which are the most important of all the constants and the most readily determined.

Wherry, in 1918, in collaboration with Yanovsky[4] made a study of the cinchona alkaloids according to this method. Yanovsky purified and recrystallized the alkaloids, crystallizing them from both benzene and alcohol, while the senior author measured the optical properties.

In 1919 the same authors[5] made an optical-crystallographic study of morphine and certain of its derivatives, namely, codeine, ethylmorphine and diacetylmorphine. Keenan and Hann[6] later recorded the optical properties of conidine hydrochloride, finding that methyl salicylate (oil of wintergreen), with an index of 1.535, was very convenient for this purpose.

In 1927, Keenan[7] determined the significant refractive indices of the following alkaloids or alkaloidal salts: brucine sulfate, morphine sulfate, atropine, diacetylmorphine, codeine sulfate, quinine sulfate and cocaine hydrochloride. Further work is being done on these alkaloids. Peterson's study[8] of ephedrine and its salts contains optical-crystallographic data on ephedrine hydrochloride and ephedrine sulfate as obtained by Walcott.

---

[1] "The Polarizing Microscope in Organic Chemistry," *Ind. Eng. Chem., Anal. Ed.*, 2 (Jan. 15, 1930), 91.

[2] *J. Am. Chem. Soc.*, 38 (1916), 1647.

[3] *Bull.* 679, U. S. Dept. Agr. (1918).

[4] *J. Am. Chem. Soc.*, 40 (1918), 1063.

[5] *J. Wash. Acad. Sci.*, 9 (1919), 505.

[6] *J. Am. Chem. Soc.*, 47 (1925), 2065.

[7] JOUR. A. PH. A., 16 (1927), 837.

[8] *Ind. Eng. Chem.*, 20 (1928), 388.

FOOD & DRUG ADMINISTRATION,
WASHINGTON, D. C.

Marked Decline in Gum Tragacanth Imports.—A decrease occurred in the importation of gum tragacanth during the 11-month period of 1930, when imports amounted to 908,179 pounds, valued at $405,127. During the same period of 1929 gum tragacanth imports amounted to 1,867,808 pounds, valued at $819,214. Gum arabic, while showing an increase in value of imports in 1930, declined 1,916,000 pounds. Imports of gum arabic during the first 11 months of 1929 and 1930, respectively, were: 8,461,152 pounds, valued at $910,893, and 6,545,149 pounds, valued at $933,836. Crude balsam imports declined during the 11-month period of 1929 and 1930, respectively, from 374,641 pounds, valued at $212,302 to 362,665 pounds, valued at $184,536.—U. S. Department of Commerce.