thought and reflection our tongues must be sober and we must tell the truth.

In conclusion, let me say that I feel this Section ought *to create a standing committee on educational policy which committee should annually or oftener make constructive recommendations to the Association looking to a rapid increase in educational requirements.* Even before establishing this proposed committee, it would be proper for this Section to recommend to the Association the adoption of a resolution advising all colleges of pharmacy to require for entrance in 1924 the completion of the first year of a standard academic college course (the first year of a Junior College) and in 1926 the completion of the second year of such a course (completion of the Junior College course). Some colleges are contemplating this step now.

It would also be consistent and proper, indeed I think called for, for this Section to advocate a professional course in pharmacy of a respectable character, quantitatively and qualitatively, covering a minimum of three years of lecture and laboratory work. I suggest that this Section go on record as advising this step forthwith. With the completion of one year of academic college work and three years of professional study the student should be entitled to the bachelor's degree in pharmacy and this degree should be required as a prerequisite to examination for license to practice. A few years hence, say a decade, the consideration of a bachelor's degree in science or art for entrance upon pharmacy should be taken up.

COLLEGE OF PHARMACY,
UNIVERSITY OF MINNESOTA.

ABSTRACT OF DISCUSSION.

LYMAN F. KEBLER: This subject has been discussed for many years; this Association should get back of the proposition for higher educational requirements of pharmacists.

E. L. Newcomb moved the appointment of a Committee in accord with the recommendation, that a standing Committee on educational policy be created, composed of five members.—Carried.

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## THE POLARISCOPE AS AN AID IN THE IDENTIFICATION OF ALKALOIDS.*

BY A. G. MURRAY.

In the qualitative analysis of a medicine of unknown composition it is usually comparatively simple to ascertain whether or not an alkaloid is present, but the identification of the alkaloid, particularly if only a small amount is available, is not always easy. There are no "group" reagents such as are used for the separation of the metals. The use of various "immiscible" solvents (*i. e.*, immiscible with water), petroleum ether, ethyl ether, benzene, chloroform, ethyl acetate, amyl alcohol, etc., does indeed permit the separation of alkaloids more or less definitely into groups. These separations are usually not sharp, however, portions of alkaloids classified with one group often being found in another. Thus it is not possible to separate quinine and strychnine quantitatively by extracting the quinine with ether.

* Contribution from Bureau of Chemistry, U. S. Department of Agriculture. Presented to Scientific Section, A. PH. A., New Orleans meeting, 1921.

A few alkaloids may be shaken out of acid solution, a fact which permits their separation from other alkaloids. The phenolic character of morphine, cupreine, cephaeline, and a few others makes possible their separation by extraction from their solutions in immiscible solvents with a solution of alkali or alkaline earth hydroxide.

Identification of alkaloids isolated in the course of analyses of medicines depends largely upon color reactions, physiological tests, and microscopic processes. For each of these tests a separate portion of the alkaloid must be used. Any characteristic property of an alkaloid which can be determined without involving the using up of the available material should therefore be taken advantage of. This will indicate what specific confirmatory tests should be applied.

The optical rotation is such a property. Most of the alkaloids are optically active.

The specific rotation of a given alkaloid in solution depends upon the solvent used, the concentration and the temperature. The influences of these conditions are so considerable as to make the use of the polariscope for exact quantitative determination of alkaloids in many cases too complicated for practical use. For example, hydrastine[1] exhibits a specific rotation of —49.8° when the solvent is absolute alcohol; it is inactive in 95% alcohol and possesses a specific rotation of +30° in 93% alcohol.

Hesse, who at one time advocated[2] the use of the polariscope in the determination of small amounts of cinchonidine in quinine, afterwards admitted[3] the practical uselessness of the method.

The effect of concentration on the specific rotation of cocaine has been studied by Antrick[4] who found that for chloroformic solutions containing from 10% to 25% of alkaloid, the specific rotation is practically constant. The same is true for nicotine[5] in benzene, ether or acetone. On the other hand, the specific rotation of nicotine in alcohol increases with the concentration of the alkaloid from —138° for the most dilute solutions to —160° for pure nicotine. With water as the solvent the effect of concentration is much greater (—75° to —160°). Carr and Pyman[6] have shown that while in chloroform the specific rotation of emetine is independent of the concentration, in 50% alcohol it increases markedly with the concentration.

Without elaborate precautions, however, data of value in the identification of an alkaloid based on optical rotation may be obtained, leaving practically all of the material originally in hand still available for confirmatory tests.

The specific rotation of an alkaloid in the free condition is usually quite different from that shown by it when in the form of a salt. Sometimes even the direction of the rotation is changed. Thus free aconitine in alcohol is dextrorotatory while aconitine hydrochloride in the same solvent is laevorotatory. The polariscope therefore permits the determination of *two* or (by the use of different sol-

[1] Carr and Reynolds, *Jour. Chem. Soc. Trans.*, 97 (1910), 1328.
[2] Liebig's *Annalen*, 205 (1880), 217.
[3] *Pharm. Jour.*, (3) 16 (1886), 818 and 1025.
[4] *Ber. d. chem. Ges.*, 20 (1887), 321.
[5] Landolt, "Optical Rotation of Organic Substances."
[6] *Jour. Chem. Soc. Trans.*, 105 (1914), 1591.

vents) even more constants of an alkaloid without using up the material itself.

In many cases, to be sure, two or more alkaloids will be found in a single medicinal preparation and unless this possibility is borne in mind incorrect deductions may be made. In these cases such separation as may be made by means of immiscible solvents or by other available methods should be resorted to. Even where separation cannot be effected one alkaloid may be present in much greater proportion than the others so that the rotation of the mixture approximates that of the preponderating alkaloid, and assists in its identification.

By the use of observation tubes of small diameter a fairly accurate approximation of the specific rotation of an alkaloid may be made when only a few milligrams of the alkaloid are available. For example, 20 mg. of emetine in 5 Cc. absolute alcohol in a 200 mm. tube gives a reading of about —0.4°, or if a Ventzke scale is used, of —1.15° V.

Polariscope tubes of the proper diameter are not listed in catalogs of chemical apparatus, although no doubt they would be made to order. A suitable tube for the purpose can be made from an ordinary 200 mm. polariscope tube (without an expanded end) by sealing within it a piece of glass tubing of 4.5–5 mm. internal diameter. If this inner tube is cut somewhat shorter than the polariscope tube a small space for a bubble is provided. Such a tube will have a volume of less than 5 Cc. The material used for sealing must be insoluble in alcohol or acidified water; litharge-glycerin mixture has been found satisfactory. Circular discs cut from a thin sheet of brass with holes of the proper diameter in the center may be fitted into the metal caps of the polariscope tube to limit the path of the light through the solution in the inner tube. A pipette similar to an ordinary medicine dropper but drawn out to a sufficient length to reach through the tube is convenient for filling; and the use of a rubber bulb on this pipette obviates the danger of drawing poisonous solutions into the mouth. The details of the procedure are as follows:

Filter the immiscible solvent containing the alkaloid through purified cotton into a small tared beaker. Evaporate the solvent at as low a temperature as practicable. (A gentle air blast is a useful aid.) Dry in a desiccator and weigh. Dissolve the residue in 5 Cc. absolute alcohol, accurately measured, keeping the beaker covered with a watch glass to prevent loss of alcohol by evaporation. Determine the rotation of the alcoholic solution in the tube above described. Return the solution as completely as possible to the beaker, rinsing the filling pipette and the polariscope tube with about 1 Cc. absolute alcohol. Evaporate the alcohol carefully, dry and reweigh the residue. If the residue weighs not more than 40 mg. dissolve in 5 Cc. 0.5% (0.1 N) sulphuric acid. Use 5 Cc. of acid of correspondingly greater concentration for residues exceeding 40 mg.

Determine the specific rotation in each solvent according to the formula

$$[\alpha]_D = \frac{100.\alpha}{l.w}$$

where $[\alpha]_D$ = specific rotation, $\alpha$ = observed rotation in angular degrees (if a Ventzke scale is used convert the reading into angular degrees by multiplying by 0.347); l = length of the tube in decimeters, and w = weight of the alkaloid in 100 Cc. (*i. e.*, 20 times the weight dissolved in 5 Cc.). Consult the table on the following page for alkaloids having approximately the specific rotations observed. Finally, reëxtract the alkaloid from the solution and apply such specific tests as may be desired.

Deviations from the procedure outlined will of course be necessary in many cases, such as for alkaloids not readily soluble in absolute alcohol or for those that decompose under the treatment described.

Possibly the procedure could be improved by acidifying the alcoholic solution instead of evaporating the alcohol, drying and reweighing the residue and taking up in acidified water. 0.1 Cc. 5 N acid would give the same acidity as 5 Cc. 0.1 N acid. Hydrochloric acid would be preferable to sulphuric for this purpose since the hydrochlorides of the alkaloids are generally more soluble in alcohol than are the sulphates. But before this procedure can be adopted it will be necessary to obtain data for the alkaloids under such conditions.

Possibly also the substitution of methyl for ethyl alcohol would be advantageous as methyl alcohol is often the better solvent. This again would require the collection of data as the literature contains but few. It is to be expected that the specific rotations in methyl alcohol will approximate the values obtained for solutions in ethyl alcohol, and this is confirmed by the meager data available (see table).

The principal difficulty encountered in the procedure outlined is in obtaining the alkaloid sufficiently free from coloring matter to permit an accurate reading of the rotation. It is often necessary to purify the alkaloid by precipitation with Wagner's or Mayer's reagent, recovering the alkaloid in the usual way. However, since purification of the alkaloid is often necessary to obtain definite color reactions and particularly for microchemical tests, it will often happen that no additional manipulation is required solely for the polarization.

If the alkaloid does not yield a clear solution with either alcohol or dilute acid, filtration through a dry asbestos mat in a Gooch crucible may be resorted to. This operation results in some evaporation of the solvent but if carefully and quickly done will give results sufficiently accurate for qualitative purposes.

The data in the appended table were compiled from the literature, with the exception of those for diacetyl-morphine which were determined by the author. With regard to some of the alkaloids the literature contains conflicting data. In a few instances the solvents used are not clearly indicated. Where the solvent used was alcohol of 95% or over the data have been recorded under the heading "In absolute alcohol." In general the presence of a small proportion of water makes no essential change in the value of rotation.

In those cases in which no data for the alkaloid in excess acid are available it has been calculated from results reported for a salt. The figures given are all calculated to the alkaloid. Some authors have used the term "basic ion" in referring to data on the salts, calculated to the alkaloid, but this of course is not

strictly accurate. Strychnine, for example, is not the basic ion of strychnine hydrochloride any more than ammonia, $NH_3$, is the basic ion of ammonium chloride ("ammonia hydrochloride").

The table is given as a compilation of the best data at present available. It is subject to correction and of course to expansion by the inclusion of data for other alkaloids. As will be noted, no data were found for several of the more important alkaloids, and for others the data are incomplete. On the other hand, data contained in the literature for some of the rare alkaloids, such as those present in comparatively small amounts in opium, have been omitted as probably of no practical value in this connection. Data for some alkaloids not known to have been used in medicines have, however, been included.

For the purpose of tabulation the alkaloids have been divided into dextrorotatory, laevorotatory and inactive in alcoholic solution. In the first and second sections the alkaloids are listed in order of their arithmetically descending specific rotations in absolute alcohol, the specific rotation in excess acid being given in the second column. Under the heading "Additional data" are given specific rotations in other solvents. At the end of each of these sections are listed alkaloids for which only the direction of the rotation is known or for which data on the salts only could be found. The optically inactive alkaloids have been tabulated in alphabetical order.

A second tabulation based on the order of magnitude of the specific rotations in excess acid solutions would be useful. It has not been given because there is not the same degree of confidence in the data for acid solutions as in that for alcoholic solutions, most of the data for acid solutions, as explained above, being based not on direct experiment but on calculations from data recorded for the salts.

No reference has been made to temperature, principally because the correction for temperature would usually be less than the experimental errors involved in the procedure in which the table is intended to be used. None of the data given is for temperatures outside the range covered by the term "room temperature." All data are for the D line.

ALKALOIDS DEXTROROTATORY IN ABSOLUTE ALCOHOL.

| Specific rotation. In absolute alcohol. | In excess acid. | Alkaloid. | Additional data and remarks. |
|---|---|---|---|
| +338 | +319 | Ergotinine | in acetone, +367; in ethyl acetate, +363; in chloroform, +396 |
| +310 | | Corydaline | in chloroform, +300 |
| +303 | | Corybulbine | |
| +283 | +186 | Corytuberine | |
| +256 | +321 | Quinidine | in methyl alcohol, +257 |
| +225 | +257 | Cinchonine | |
| +174 | +215 | Oxyacanthine | |
| +121 | +47 | Cinchonamine | |
| +115 | | Chelidonine | |
| +113 | | Glaucine | |
| +63 | | Quebrachine | in chloroform, —19 |

| Specific rotation. In absolute alcohol. | In excess acid. | Alkaloid. | Additional data and remarks. |
|---|---|---|---|
| +51 | +114 | Yohimbine | |
| +45 | | Ergotoxin | Behavior erratic[1] |
| +45 | | Myoctonine | |
| +42 | | Lycaconitine | |
| +24 | —27 | Japaconitine | |
| +22 | | Carpaine | |
| +19 | —22 | Pseudaconitine | |
| +18 | —18 | Indaconitine | |
| +12 | —15 | Bikhaconitine | |
| +11 | —37 | Aconitine | |
| +10 | | Conhydrine | |
| +8 | 0 | Coniine | |
| +8 | —41 | Pelletierine | |
| | +116 | Ergothioneine | in water, +110 |
| | +108 | Pilocarpidine | in water, +101 |
| | +97 | Pilocarpidine | in water, +81 |
| | +46 | Isopilocarpine | in water, +43 |
| | +27 | Methyl pelletierine | |
| | +5 | Dioscorine | |
| | +3 | Gelsemine | in chloroform, +16 |
| | | Bulbocapnine | in chloroform, +237 |
| | | Corydine | in chloroform, +204 |
| | | Corycavamine | in chloroform, +167 |
| | | Hydroxylupanine | in water, +64 |
| | | Vellosine | in chloroform, +23 |
| **Alkaloids Laevorotatory in Absolute Alcohol.** | | | |
| —315 | | Stylopine | |
| —298 | | Bebeerine | |
| —288 | | Echitamine | |
| —216 | —198 | Thebaine | |
| —185 | +50 | Narcotine | in chloroform, —207 |
| —180 | —170 | Diacetyl-morphine | in methyl alcohol, —176; in ethyl alcohol & excess acid, —148; in methyl alcohol & excess acid, —153 |
| —175 | —283 | Cupreine | |
| —170 | | Anagyrine | |
| —168 | —276 | Quinine | in 50% alcohol, —171; in 50% alcohol & excess acid, —262 |
| —141 | —123 | Morphine | in methyl alcohol, —139 |
| —138 | +21 | Nicotine | in water, —75. Data is for very dilute solutions |
| —136 | —133 | Codeine | in water, —144; in chloroform, —111; in 50% alcohol & excess acid, —134 |
| —128 | —34 | Strychnine | in amyl alcohol, —233 |
| —108 | —178 | Cinchonidine | in chloroform, —86 |
| —100 | —62 | Aspidospermine | in chloroform, —84 |

[1] Berger and Carr, *Jour. Chem. Soc. Trans.*, 91 (1907), 337.

| Specific rotation. In absolute alcohol | In excess acid. | Alkaloid. | Additional data and remarks. |
|---|---|---|---|
| —93 | | Geissospermine | |
| —89 | —153 | Physostigmine | |
| —85 | —34 | Brucine | in chloroform, —127 |
| —80 | | Senecionine | |
| —72 | | Aspidospermatine | |
| —50 | +158 | Hydrastine | in 50% alcohol, +115<br>in 50% acetone, +100<br>in pure acetone, —85<br>in chloroform, —64<br>in 50% alcohol neutralized with HCl, +197 |
| —50 | | Paytine | |
| —48 | | Ibogaine | |
| —35 | | Imperialine | |
| —35* | —81 | Cocaine | in chloroform, —16; in 50% alcohol & excess acid, —79 |
| —34 | | Echitamine (Ditaine) | |
| —26* | +26 | Emetine | in chloroform, —50 |
| —21 | | Pseudohyoscyamine | |
| —20 | —32 | Hyoscyamine | in 50% alcohol, —22; in 50% alcohol & excess acid, —27 |
| —20 | +33 | Atisine | |
| —19 | —17 | Lupinine | |
| —18 | —33 | Hyoscine | in water, —28 |
| —16 | | Sparteine | |
| | —116 | Cytisine | in water, —120 |
| | —68 | Ecgonine | |
| | —45 | Ephedrine | |
| | +34 | Cephaeline | in chloroform, —43 |
| | | Anhalonine | |
| | | Colchicine | in chloroform, —121<br>in water, —429 |
| | | Samandarine | in water, —54 |
| | | Ibogine | in benzene, —13 |

ALKALOIDS OPTICALLY INACTIVE IN SOLUTION.

| | | |
|---|---|---|
| Anhalamine | Delphinine | Piperine |
| *Anhalonidine | Echinopsine | Pseudopelletierine |
| Atropine | Harmaline | Samandaridine |
| Berberine | Harmine | Sanguinarine |
| Caffeine | Homatropine | Staphisagrine |
| Chelerythrine | Hydrastinine | Theobromine |
| Chrysanthemine | Isopelletierine | Tropine |
| Corycavine | Narceine | Veratrine |
| Curarine | Papaverine | |

* In 50% alcohol.