phases only, unless we suppose a fifth for the eighth group. If the motion of an atom can be changed from one character to another its valence is changed and in such general properties as are dependent upon motion and not upon atomic weight it is equivalent to changing its group. Electricity, light, heat, and chemical action can cause this change of motion. In so far the properties of the element are subject to change and within our control. But the other factor, atomic weight, with the properties of the element determined by it, is not subject to change nor within our control, so far as our knowledge goes.

While it is freely granted that there is so much of the speculative in what has been said as to make us touch the whole subject with extreme caution, and while it is further admitted that it is quite beyond the reach of present experimental research, yet it is believed that the use of the imagination is legitimate and tends toward the advancement of the science so long as the true value is set upon it and fancy is not allowed to obscure fact nor to be mistaken for it. The hypothesis proposed is simple and if true will be very helpful. It will be a great step forward if it can be shown that the doctrine of valence is a doctrine of vibratory equilibrium.

EMETINE OCTOIODIDE AND THE EXTRACTION AND ESTIMATION OF ALKALOIDS GENERALLY.[1]

BY H. M. GORDIN AND A. B. PRESCOTT.

Received November 27, 1898.

IN a previous paper[2] we have shown that most alkaloids form definite compounds when treated with excess of iodopotassium iodide and that it is possible to estimate the strength of aqueous solutions of alkaloidal salts by means of standardized solutions of iodine and of sodium thiosulphate. In applying this method to the assay of medicinal drugs it is immaterial what method of extraction of the alkaloids from the drug is employed, provided the final alkaloidal solution be sufficiently deprived of non-alkaloidal matter. The simplest and quickest method of obtaining the alkaloidal solution sufficiently free from foreign

[1] In the work of Research Committee D, Section 2, Committee of Revision and Publication of the Pharmacopoeia of the United States. Read by title before the New York meeting of the American Chemical Society, December 28, 1898.

[2] This Journal, 20, 706, Sept., *1898*.

matter is undoubtedly the method proposed by Dr. A. B. Lyons.[1]

This consists in macerating a weighed quantity of the powdered drug in a definite volume of Prollius' fluid with frequent shaking for several hours, drawing off an aliquot part of the clear liquid, evaporating and taking up the residue with acidulated water. The alkaloidal solution obtained by this method is generally almost perfectly colorless and can be worked up further for a gravimetric estimation by shaking out the alkaloids with chloroform and ammonia. For our iodometric method the filtered solution can be treated directly with excess of iodine, the excess of which is then estimated by sodium thiosulphate. For the alkalimetric estimation, again, the same filtered solution may be taken, using standardized acid in excess and estimating the excess by means of standardized alkali. The only drawback to this method of extraction is the great difficulty of preventing loss by evaporation of the highly volatile solvent, by which loss the volume of the aliquot part becomes reduced, and the final figure is liable to be too high.

A GENERAL METHOD OF EXTRACTION.

In order to avoid this difficulty we have worked out an entirely different method of alkaloidal extraction which can also be used with any one of the methods of estimation as desired. In its main features this method is the same as that which we proposed for the assay of opium.[2] It is carried out in the following manner :

One to four grams of the finely powdered drug is weighed into a low wide-mouthed vessel, with a round bottom, holding eight or ten ounces and having a well-fitted cork, such as a screw-top ointment-jar.[3] The powder is rubbed up with a small pestle to a fine paste by adding a little of a solvent mixture, composed of stronger ammonia water and alcohol each five cc., chloroform ten cc., and ether twenty cc. Then a few more cubic centimeters of this mixture are added, so as to have the drug well covered with the liquid, using in all about five times the amount of the drug taken. The vessel is corked, with the pestle inside, and is set aside for about four or five hours, taking care to agitate by

[1] Manual of Pharm. Assaying, Haynes & Co., Detroit, Mich., *1886*, p. 20.

[2] This Journal, *1898*, **20**, 724; *Pharm. Archives*, *1898*, p. 121.

[3] An ordinary teacup fitted with a specie cork answers well.

circular movement very frequently during that interval. After that time the cover is removed and the vessel kept in a current of air, stirring frequently till all odor of ammonia has disappeared. With a good draught and frequent stirring the powder will be almost perfectly dry in about two hours. The vessel is then put into a vacuum desiccator over sulphuric acid for about four or five hours.

An amount of powdered sodium chloride equal to about five or six times the amount of drug employed is then carefully mixed in, with use of the pestle, and the whole thrown into a small percolator, one provided with a glass stop-cock and having a plug of cotton at the bottom.[1] The vessel is then cleaned out several times with small quantities of sodium chloride, and the cleanings added to the percolator. The mixture in the percolator is then covered with a piece of cotton which is pressed down with a piece of glass, and a suitable menstruum, usually chloroform, is poured slowly into the percolator till the menstruum reaches the stop-cock. The latter is then closed, the percolator covered, and set aside for five or six hours. After that time the stop-cock is opened, and the drug exhausted with the menstruum percolating until ten drops of the percolate being evaporated on a watch-glass, and the residue taken up with a few drops of acidulated water, the solution shows no turbidity whatever on adding a few drops of Wagner's reagent. When finished the percolate, which is received in a flat evaporating dish, is placed in a good draught at a temperature of about 30° C. When the liquid is reduced to a very small volume, ten cc. of acidulated water[2] are added, and then a few cubic centimeters of ether, or petroleum ether, so as to have an ethereal liquid cover the aqueous solution,[3] when the whole is stirred with a glass rod until all the ethereal liquid is driven off. The liquid is then filtered and the evaporating dish and filter washed several times with acidulated water. In this way is obtained a colorless solution of the alkaloid, which can be worked up for any method of assay.

[1] A suitable percolator is easily made out of an ordinary piece of glass tubing fitted with a perforated cork through which passes a tube having a glass stop-cock.

[2] If an alkalimetric assay is intended the acidulated water in the operation should be standardized and taken in definite quantities.

[3] If the menstruum is all evaporated off it is sometimes difficult to dissolve out the alkaloids with acidulated water. If chloroform be used, coming below the aqueous layer, it evaporates too slowly.

THE IODOMETRIC ESTIMATION.

In the periodide method of assay the final alkaloidal solution obtained, whether by our method, by Dr. Lyons' method, or by any other method, this final solution representing a definite quantity of the drug to be assayed, is poured slowly and with constant stirring into a flask holding 100 cc. in which has been previously drawn twenty or thirty cc. of a standardized solution of iodine and one or two cc. of dilute hydrochloric acid[1] (U. S. P.). The flask is then filled up to 100 cc., stoppered, and well shaken till the periodide has separated out. The supernatant liquid is to be perfectly transparent but of a red iodine color. Fifty cc. are then filtered off and in this portion the excess of iodine determined by means of standard sodium thiosulphate. The amount of iodine consumed multiplied by the suitable factor, gives the amount of alkaloid present in the quantity of drug taken.

In the case of several alkaloids being present in the drug a mean iodometric factor can be deduced in the same way as is done in the alkalimetric assay. It is to be noticed that should there be no precipitate with iodine, but only a slight turbidity, then the drug is extremely poor and for the assay a much larger quantity than one to four grams should be taken. On the other hand should the supernatant liquid, after adding the alkaloidal solution to the iodopotassium iodide solution and separating the periodide by shaking, have very little color or be almost colorless then it is certain that the drug is very rich, and either a smaller quantity of the drug or a larger quantity of the iodine solution must be employed in the assay.

The method of extraction described above presents particular advantages in those cases where several alkaloids soluble in different menstrua are present in the drug, as by using these menstrua successively, a separation of the alkaloids can be easily effected. This principle we have applied to the assay of opium, and it seems also to be applicable to *Hydrastis canadensis*, a report upon which we intend to publish in the near future.

This method of extraction of alkaloids for assay purposes has given us very good results with all drugs experimented upon,

[1] Except in the case of morphine an excess of acid is not hurtful and even promotes the separation of the periodide. Hydrochloric is to be preferred to sulphuric acid.

except ipecac root. For some unaccountable reason it is almost impossible to extract free emetine, which is liberated in our process by the ethereoammoniacal mixture, from this root by percolation. Ether, chloroform, and acetone were tried as menstrua, but in all cases the result was much lower than that obtained by Lyons' process.[1] Though the percolation was not interrupted till a few drops tested in the general way with Wagner's reagent gave no reaction whatever. The very low result as compared with that obtained by Lyons' method shows conclusively that the exhaustion cannot be made complete by percolation. This fact would possibly explain why Flückiger[2], who extracted ipecac by percolation with ammoniated chloroform, obtained exceptionally low results.[3] In the assay of ipecac, given at the end of this paper, the method used was that of Dr. Lyons. The other drugs have been extracted by our method as described above, and the results compared with those obtained by Lyons' method.

The periodide assay method applied to nux vomica, along with a modification of Dunstan and Short's method of separation of strychnine from brucine[4] affords a convenient way of separate estimation of each of these alkaloids in the drug as follows:

The acidulated alkaloidal solution obtained from nux vomica in any suitable way, and representing four grams of the drug, is made up to a definite volume, say 100 cc. Of this solution twenty-five cc., which represent one gram of nux vomica, are run from a burette into a 100 cc. flask in which has been placed twenty cc. of decinormal iodine solution and two cc. dilute hydrochloric acid, and the amount of iodine consumed by the total alkaloids contained in that one gram nux vomica is reached in the way described above. Let that amount be *a*. If only the amount of total alkaloids in the nux vomica is desired it is sufficient to multiply *a* by 47.845 which is equal to 100 times the mean factor of strychnine and brucine and the percentage of total alkaloids is at once obtained.

THE SEPARATE ESTIMATION OF STRYCHNINE AND BRUCINE.

For the separate estimation of each of these alkaloids, another

[1] It is Lyons' general method, not his modification of Dragendorff's method, that is referred to here.

[2] *Pharm. Ztg.*, *1886*, 30.

[3] See also Guareschi: Einfeuhr in d. Stud. d. Alkal., *1896*. 527.

[4] *Pharm. J. Trans.* (3), 14, 290; *Am. J. Pharm.*, *1883*, 579.

portion of the alkaloidal solution, representing two grams of the nux vomica, that is fifty cc., is run out from the burette into an Erlenmeyer flask of the capacity of about 300 cc. and to the contents of the flask ten cc. of a two per cent. solution of sulphuric acid is added, and then water enough to make in all about 200 cc. Then pour in twenty-five cc. of a five per cent. solution of potassium ferrocyanide, stopper the flask and shake continuously for about half an hour. Now filter, wash the precipitate on the filter repeatedly with water containing one per cent. of sulphuric acid, till a few drops of the filtrate diluted with a little water have no bitter taste. The filter is then pierced and the precipitate rinsed with use of the wash-bottle into a 100 cc. flask. To the contents of the flask are then added twenty cc. of a five per cent. solution of zinc sulphate, and the flask kept on a boiling water-bath for about fifteen minutes. The zinc sulphate decomposes the strychnine ferrocyanide, zinc ferrocyanide is precipitated, and strychnine sulphate remains in solution. The flask is then completely cooled, and water enough added to make 100 cc. Of this, fifty cc. representing again one gram of the nux vomica but deprived of the brucine, are then filtered off and run out from the burette into a 100 cc. flask containing twenty cc. decinormal iodine solution, and about two cc. of dilute hydrochloric acid. The amount of iodine consumed by the strychnine alone is then determined as above. Let it be b. Then $b \times 43.9$ (100 times the strychnine factor) gives the percentage of strychnine, and $(a - b) \times 51.79$ is the percentage of brucine in the nux vomica.

To test the exactness of this method we prepared a solution containing known quantities of each of these alkaloids and determined these by the described method. The results as can be seen from the following table are fairly satisfactory, if we consider the well-known difficulties of this separation.

The solution contained 0.16 per cent. strychnine and 0.22 per cent. brucine (anhydrous).

	Iodine consumed by 10 cc. before the removal of brucine.	Iodine consumed by 10 cc. after the removal of brucine.	Found. Strychnine.	Found. Brucine.	Contained. Strychnine.	Contained. Brucine.
1	0.0843132	0.032397	0.14	0.24	0.16	0.22
2	0.0843130	0.032397	0.14	0.24	0.16	0.22

Following is a report of drugs which we have so far assayed

both gravimetrically and iodometrically. The factors are those given for the higher periodides in our previous paper.[1] For nux vomica the mean factor was taken which is equal to 0.47845 parts of total alkaloids for one part iodine consumed. For ipecac root the factor 0.5453 is used which is based upon the fact that, as shown at the end of this paper, emetine forms a hydriodide heptiodide when treated with excess of iodopotassium iodide.

Taking Lefort and Wurtz's formula for emetine we get

$$7 \times 126.53 : 482.98 :: 1 : \text{factor} = 0.5453.$$

The factors for the drugs of the table are as follows:

Mean factor of strychnine and brucine	0.47845
Atropine	0.2849
Emetine	0.5453

Drug.		Quantity taken for assay. Grams.	Iodine consumed.	Percentage of alkaloids. Iodometric.	Gravimetric.
NUX VOMICA.					
Iodometric	1	1	0.0526816	2.52	....
	2	1	0.0526725	2.52	....
Gravimetric	1	1	*	....	2.73
	2	1	*	....	2.73
BELLADONNA ROOT.					
Iodometric	1	2.5	0.0459179	0.52	....
	2	2.5	0.0459263	0.52	....
Gravimetric	1	2.5	*	....	0.51
	2	2.5	*	....	0.51
BELLADONNA LEAVES.					
Iodometric	1	5	0.0478286	0.27	....
	2	5	0.0475922	0.27	....
Gravimetric	1	5	*		0.28
	2	5	*		0.28
IPECAC ROOT.					
Iodometric	1	2	0.0957764	2.61	....
	2	2	0.0986633	2.69	....
Gravimetric	1	2	*		2.63
	2	2	*		2.62

* Alkaloids shaken out and weighed.

Emetine Octoiodide.

Emetine seems to form with iodine two periodides, according to whether the iodine is added to the alkaloid or *vice versa*, but owing to the lack of material we have only isolated and analyzed

[1] This Journal, (*1898*), **20**, 724.

one; namely, the higher periodide. The emetine used was obtained from Merck & Co. The periodide was made by pouring 200 cc. of a solution of emetine in acidulated water, this solution containing about half a per cent. of the alkaloid, into about 500 cc. of a solution which contained about one per cent. of iodine with one and five-tenths per cent. of potassium iodide, and was strongly acidulated by hydrochloric acid. The mixture was shaken till the supernatant liquid became perfectly transparent, the precipitate was separated by means of the pump, quickly washed with cold water and then dried, first on porous plates and then *in vacuo* over sulphuric acid.

Thus obtained the periodide is a dark-brown powder, hardly soluble in benzene, ether, or chloroform, quite soluble in alcohol, and very soluble in a mixture of four parts of alcohol and one of chloroform. The chloroform greatly increases the solubility of the periodide in alcohol, though chloroform alone hardly dissolves it. So far we have not been able to recrystallize it. On evaporation of the solvent a viscous mass is generally left. Authorities differ with regard to the formula of emetine, as follows:

Lefort and Wurtz,[1]	$C_{28}H_{40}N_2O_5 = 482.98$
Glenard,[2]	$C_{30}H_{44}N_2O_4 = 494.96$
Kunz,[3]	$C_{30}H_{40}N_2O_5 = 506.92$
Paul and Cownly,[4]	$C_{15}H_{22}NO_2 = 247.48$

Our periodide corresponds best to the formula of Lefort and Wurtz. It seems to be an emetine hydriodide heptiodide, $C_{28}H_{40}N_2O_5.HI.I_7$.

For the estimation of the additive iodine the periodide is dissolved in chloroform mixed with alcohol and titrated with standardized sodium thiosulphate using starch as indicator. It is best to add first an excess of the thiosulphate solution, then add considerable water, when the excess is titrated back with standardized iodine. For the total iodine the periodide is dissolved in a little chloroform mixed with a few drops of alcohol; powdered zinc is then added and the mixture kept on a water-bath till effervescence (from the action of zinc on the chloroform)

1 *Ann. chim. phys.* (5), **12**, 247.
2 *Ibid.* (5), **8**, 233.
3 *Arch. d. Pharm.*, **225** (*1887*), 461; **232** (*1894*), 466.
4 *Pharm. J.*, (3), **24**, 61.

ceases. To the mixture, when cold, ammonia water is added, and the iodine in the zinc and ammonium iodide is estimated exactly as described in the analysis of morphine tetraiodide.[1]

For additive iodine 0.1492 gram of the periodide gave 0.0880045 gram iodine, and 0.122 gram gave 0.0727250 gram iodine.

	Calculated for $C_{28}H_{40}N_2O_5.HI.I_7$.	Found.
1	59.24	59.98
2	59.24	59.61

For total iodine 0.1313 gram of the periodide gave 0.0890502 gram iodine, and 0.12095 gram gave 0.0818797 gram iodine.

	Calculated for $C_{28}H_{40}N_2O_5.HI.I_7$.	Found.
1	67.69	67.82
2	67.69	67.69

CHEMICAL LABORATORY OF THE
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NOTES ON THE RAPID DETERMINATION OF TUNGSTEN IN STEEL.[2]

BY GEORGE AUCHY.

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THE rapid method of determining tungsten in steel, generally in use and described in Blair's "Chemical Analysis of Iron," is as follows: Solution of the steel in aqua regia; evaporation to dryness; re-solution in strong hydrofluoric acid containing a little strong nitric acid; dilution and boiling; filtration and ignition of the tungstic oxide contaminated with silica and ferric oxide; elimination of the silica by hydrofluoric acid; ignition and weighing of the tungstic acid and ferric oxide; fusion with sodium carbonate; solution and filtration to determine the ferric oxide. If in this method the final steps—the fusion with sodium carbonate and the determination of the ferric oxide—could be dispensed with, evidently a very considerable saving of time and trouble in the performance of the method would be made; and it has doubtless been observed by many members of the society having occasion to make tungsten determinations in steel, that within the range of their experience the ferric oxide thus carried down with the tungstic acid is constant in amount or nearly so. If this uniformity exists in all steels containing every percentage of tungsten, of course, the determination of

[1] This Journal, *1898*, **20**, 717.

[2] Read by title before the New York meeting of the American Chemical Society, December 28, 1898.