NOTES ON THE STABILITY OF GLYCERITE OF BISMUTH AND ITS EFFECT ON ELIXIR PEPSIN AND BISMUTH N. F. IV.*

BY K. A. BARTLETT.

In the preparation of **Glycerite of Bismuth** N. F. IV some difficulty is experienced in obtaining a stable preparation and one that will contain the required amount of Bismuth Oxide. Similarly it is found that **Elixir Pepsin and Bismuth** N. F. IV prepared from this glycerite is not stable and deposits a granular precipitate on standing.

In preparing **Glycerite of Bismuth** in accordance with the N. F. IV formula it is found that upon adding the tartaric acid powder to the solution of bismuth subnitrate in nitric acid and distilled water, it is impossible to get the material all in solution, an insoluble precipitate remaining which causes the resulting glycerite to assay low in bismuth oxide. A change in procedure here whereby the tartaric acid is first dissolved in the distilled water and this solution then added slowly and with constant stirring to the solution of bismuth subnitrate in nitric acid, eliminates this difficulty and a glycerite results that will assay up to the required standard.

This, however, does not eliminate all the trouble. A glycerite so made will assay up to the standard when freshly prepared but will soon begin to precipitate with a gradual loss in bismuth content. It was found that this was due to the washing of the magma not being carried far enough. The N. F. IV directs the washing to be continued until the wash water has but a slight saline taste. If only carried this far, the precipitation mentioned above will take place. If, however, the washing is carried on until the wash water no longer responds to the test for nitrates, the difficulty is overcome and a preparation is obtained that is apparently stable.

A sample of glycerite and an elixir made from it have been under observation for eighteen months and both are clear and show no sign of precipitation. The glycerite assayed 12.9 Gm. of Bismuth Oxide per 100 cc. when made and a recent check assay showed 12.808 Gm. Since the glycerite shows no sign of precipitation this slight difference is attributed to experimental error.

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A NOTE ON THE ASSAY OF TINCTURE OF HYOSCYAMUS.*

BY WILLIAM F. REINDOLLAR.

The United States Pharmacopœia recognizes thirty-two galenicals which are subject to alkaloidal assay. These preparations vary in strength from the **Extract of Opium** which heads the list with a 20% alkaloidal content down to the **Tincture of Hyoscyamus** containing the modest quantity of 0.0065 Gm. alkaloids per 100 cc. or approximately 0.0065%. This variation is due to several factors, such as, the amount of alkaloid occurring in the plant, the potency of

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these active constituents, the type of preparation (*i. e.*, extract, fluidextract, or tincture); the therapeutic properties of the drug, etc., and need not be discussed here. Suffice it to say that the alkaloidal content of **Tincture of Hyoscyamus** is proportionate to that of the other Hyoscyamus preparations and is suitable in amount to the purposes for which the Tincture is used.

It is the absolute quantity of alkaloid present, however, with which this paper is concerned. This amount is so minute that it is difficult to obtain closely agreeing results by the pharmacopœial method. Let us consider the quantity present and make a few comparisons. The U. S. P. IX states that "One hundred mils of **Tincture of Hyoscyamus** yields not less than 0.0055 Gm. nor more than 0.0075 Gm. of the alkaloids of Hyoscyamus." Comparatively speaking, this is but one-half the alkaloidal content of **Tincture of Physostigma,** one tenth that of **Tincture of Aconite** and only about one fortieth that of **Tincture of Nux Vomica.** In terms of the volumetric solution used to dissolve it, the alkaloid is entirely represented by 0.25 cc. $N/10$ H_2SO_4. An error, therefore, of one drop (0.05 cc.) in the measurement of the acid would make an error approximating 20% in the result. The Pharmacopœia realizing this directs that the excess acid be titrated with a very weak alkali, namely $N/50$, in order that the end-point may be approached cautiously and the danger of over-titrating reduced to a minimum.

In order to eliminate, as much as possible, various sources of error the following precautions were observed. The tinctures were concentrated at an approximate temperature of 90° C. instead of the conventional water-bath heat, each step of the shaking out process was checked with Mayer's Reagent and the alkali solution was restandardized before every titration. The acid used was $N/10$ H_2SO_4 gravimetrically standardized in the usual manner and measured from a small calibrated burette capable of being read to $^1/_{200}$ cc. The alkali solution was protected from carbon dioxide and was also delivered from a calibrated burette. A dilution of methyl red, the indicator used, was kept nearby as a comparator for the end-point, the titration being carried to an intermediate orange tint instead of lemon yellow. An effort was made to maintain as far as possible a uniform working temperature. In spite of these precautions the results were not as satisfactory as might have been expected. While duplicate determinations agreed fairly well in the majority of cases, there were still some inexplicable discrepancies, and when the figures of different analysts were compared there was found a wide variation in the results. The tables below will serve as an illustration.

After a dozen or more samples had been assayed, a standard tincture was prepared and portions delivered to three analysts, one to a Philadelphia chemist known to be an expert in alkaloidal work, another the Chief Chemist of a pharmaceutical manufacturing house, the third an analyst at this Bureau. These men were aware of the discrepancies mentioned above and, therefore, exercised additional care in their analyses. The results:

TINCTURE OF HYOSCYAMUS.

Chemist A (Philadelphia)	0.00388	0.00374
Chemist B (Manufacturing House)	0.0072	0.0079
Chemist C (Bureau of Chemistry)	0.00451	0.00457

It will be noted that each chemist checks himself fairly well, but that there is very little agreement between any pair of results. While the highest result recorded is more than double that of the lowest, making a comparative error over 100%, and while the figures reported extend beyond both the minimum and maximum limits of the Pharmacopœia, it must be borne in mind that the total absolute difference is less than $^1/_{15}$ grain—a check that, in the assay of other alkaloidal drugs, would be considered close agreement indeed.

The results recorded below were obtained from galenicals purchased in the open market and assayed previous to the standard tincture.

TINCTURE OF HYOSCYAMUS.

	Chemist C.		Chemist B.		Chemist D.*
1	0.0039	0.0038			
2	0.0043	0.0058			
3	0.0055	0.0060			
4	0.0032	0.0043			
5	0.0060	0.0063			
6	0.0042	0.0039			0.0044
7	0.0052	0.0058			0.0051
8	0.0052		0.0075	0.0082	
9	0.0046		0.0072	0.0062	

* Analyst at Federal Food and Drug Control Laboratory.

Conclusion—It appears that the Proximate Assay method prescribed by the U. S. P. for its alkaloidal preparations is not sufficiently accurate when used to standardize a galenical containing such a minute quantity of alkaloid as the Tincture of Hyoscyamus.

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THE ALLEGED INCOMPATIBILITY OF ACID SODIUM PHOSPHATE AND METHENAMINE.*

BY BERNARD FANTUS AND CLYDE M. SNOW.

Methenamine and Acid Sodium Phosphate are frequently given alongside of each other so as to acidify the urine and in this manner secure the liberation of formaldehyde, upon which its activity as a urinary antiseptic depends. It is generally advocated that the two be given separately, so as to avoid the premature liberation of the formaldehyde by the acid sodium phosphate.

Attention is called by a correspondent in the *Journal of the American Medical Association* (vol. 85 (July 18) 1925, pp. 214, 215) to the fact that in the Pharmacopœia of the London Hospitals there appears a mixture under the name of "Mistura Hexaminæ" containing both methenamine and acid sodium phosphate combined. In view of the fact that it is sometimes quite an inconvenience for a patient to carry with him two separate bottles of medicine, the question as to the degree of incompatibility of the two agents, and the desirability of the formulas given in the "London Hospitals' Formulary" becomes of practical interest.

* Section on Practical Pharmacy and Dispensing, A. PH. A., Des Moines meeting, 1925.