

Rosenthaler, L.

**Synthetic menthol**

*Pharm. Zentralh.* (March 12, 1925); through  
*Chem. & Drug.*, 102 (1925), 450

Sen, Rajendra Nath, and Sarkar, Nripendra  
Nath

**Condensation of primary alcohols with resorcinol and other hydroxy aromatic compounds**

*J. Am. Chem. Soc.*, 47 (1925), 1079

Schulek, E.

**Berlin blue test for hydrocyanic acid**

*Pharm. Ztg.*, 70 (1925), 153

Snell, Foster D.

**Laboratory production of viscose**

*Ind. & Eng. Chem.*, 17 (1925), 197

Strobinger, R., and Streit

**Estimation of glycerin by oxidation with potassium and sulphuric acid**

*Pharm. Ztg.*, 70 (1925), 119

Tarugi, N.

**Study of a reaction of formic aldehyde**

*Boll. Chim.-Farm.*, 63 (1924), 337; through *Bull. Sci. pharmacol.*, 32 (1925), 188

Thoms, H.

**Detection of diethylphthalate in alcohol**

*Apoth.-Ztg.*, No. 95 (1924); through *Pharm. Ztg.*, 70 (1925), 119

Vanino, L., and Herzer, F.

**Preparation of acetylsalicylic acid peroxide**

*J. pharm. Belg.*, 7 (1925), 45

Voorhees, Vanderveer, and Skinner, Glenn S.

**Some new derivatives of barbituric acid**

*J. Am. Chem. Soc.*, 47 (1925), 1124

Zamparo, Aldo

**Differentiation of naphthol and the condensation product of  $\alpha$ -naphthol and formaldehyde**

*Boll. Chim.-Farm.*, 64 (1925), 97

CLINICAL AND DIAGNOSTIC  
METHODS.

Benguereel, C.

**Determination of chlorides in blood**

*Répert. pharm.*, 36 (1925), 67

Benguereel, C.

**Detection of urobilin and urobilinogen in urine**

*Répert. pharm.*, 36 (1925), 65

THE ARSENICAL SOLUTIONS.

No. 2.\* *Liquor Acidi Arsenosi (De Valangin's Solution).*

BY H. A. LANGENHAN.\*\*

*History and Original Formulas.*—According to Pereira<sup>1</sup> Dr. De Valangin, a Swiss physician practicing in London, introduced the *solutio solventis mineralis* into medical practice. Inasmuch as De Valangin died in 1805, this must have been done not long after Fowler's Solution made its appearance in 1783.

According to Dr. Withering<sup>2</sup> an aqueous solution of arsenic trioxide had been used under his supervision, but this solution decomposed. Hence he discontinued its use and substituted Fowler's Solution in its place. So little is known about De Valangin's work that it does not become apparent whether he attempted to make a more stable solution by adding the hydrochloric acid, whether he desired an acid solution in distinction to Fowler's alkaline solution, or whether he thought he had a distinctively new preparation.

This much becomes apparent from Pereira's account, that he sublimed a mixture of "arsenious acid" and "common salt," that the sublimate was designated as

\* For No. 1 see "Trans. Wisc. Academy of Sciences, Arts and Letters," v. 20, or Bull. U. of Wisc., "Liquor Potassii Arsenitis".

\*\* Associate Professor of Pharmacy, College of Pharmacy, University of Washington, Seattle.

<sup>1</sup> *Pharm. Jour.*, 8, p. 395 (1849).

<sup>2</sup> See Fowler's report, "Trans. Wisc. Academy of Sciences, Letters and Arts," v. 20.

"solvent mineral" and that his "solution of solvent mineral" was made by dissolving the sublimate in diluted hydrochloric acid. We are also told by Pereira that De Valangin presented the "Apothecaries Company with a quantity of his preparation, as well as with the formula for its manufacture." Thus it evidently came into general use.

That the "arsenious acid" does not undergo a chemical change when sublimed with sodium chloride, is pointed out by Pereira, who also states that, "The solution of solvent mineral is by some persons regarded as a solution of chloride of arsenic. Hence when its introduction into the London Pharmacopœia was proposed the following formula was suggested by Mr. Warrington; Arsenious acid, gr. XXX; Hydrochloric acid, gr. XC; Distilled water, f. oz. XX. Dissolve the arsenious acid in the hydrochloric acid diluted with about 1 f. oz. of water; then add the remainder of the water to the solution." The chemistry of the reaction is explained by Pereira in the following words: "By dissolving the arsenious acid in the hydrochloric acid we obtain a solution of, either of the terhydrochlorate of arsenious acid or the terchloride of arsenic,  $As_2O_3 + 3HCl = AsCl_3 + 3HO$ ." He substantiates this by pointing out that "According to Duparquier<sup>1</sup> the solution contains terchloride of arsenic."

Such was the state of our knowledge concerning this solution in 1849, at the time when the secret<sup>2</sup> preparation of the Apothecaries Company was considered for admission into the London Pharmacopœia in which it was made official in 1851 as *Liquor Arsenici Chloridi*. The first revision of the U. S. P. to adopt this solution was that of 1870. It applied to it the title of *Liquor Arsenici Chloridi*, the title of the London Pharmacopœia rather than that of the British Pharmacopœia being adopted. It has continued being official in both of these national standards, but has not found its way into other Pharmacopœias.

#### COMMENTS ON THE PHARMACOPŒIAL TEXT.

##### *Introductory Statement.*

Although De Valangin's solution was introduced into the medical practice soon after Fowler's solution made its appearance, it was not made official in the United States Pharmacopœia until 1870. Hence there are but five written texts to be considered. Again as with Fowler's solution, the detailed comments on the text, whether based on the study of the literature of the subject, or on laboratory experiments or observations, are recorded in connection with those parts of the text to which they have reference. A better oversight over this part may be had by a mere glance on the text subjects commented upon:

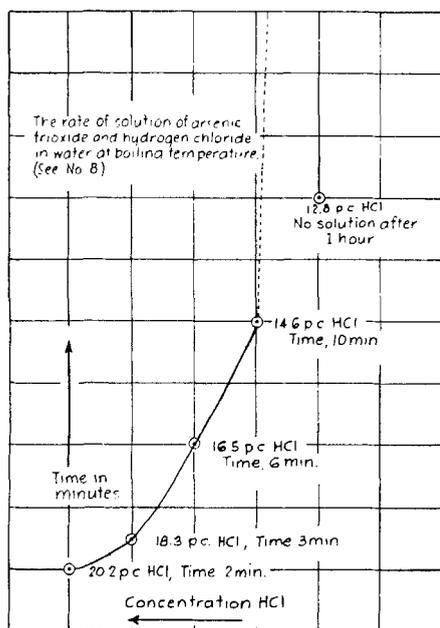
- |  |                                    |
|--|------------------------------------|
| 1. Titles and synonyms                     | 8. Solution of arsenic trioxide    |
| 2. Definition                              | 9. Volume of finished product      |
| 3. The form of arsenic trioxide used       | 10. Appearance of finished product |
| 4. Hydrochloric acid as an ingredient      | 11. Qualitative tests              |
| 5. Ratio of ingredients                    | 12. Assay                          |
| 6. Water                                   | 13. Dose                           |
| 7. Amount of water used to effect solution |                                    |

<sup>1</sup> *Jour. de Pharm.*, 27, p. 717 (1841).

<sup>2</sup> *Pharm. Jour.*, 2, p. 112.

1. *Titles and Synonyms.*—Dr. De Valangin first prepared his arsenical solution by subliming a mixture of “arsenious acid” and “common salt.” The sublimate was called *Solvent mineral*. This was dissolved in diluted hydrochloric acid, and formed his *Solution of solvent mineral* or *Solutio Solventis Mineralis*. This title was probably used to differentiate this preparation from the alkaline solution of Fowler, which was introduced under the title *Mineral Solution* or *Solutio Mineralis*. The London Pharmacopœia of 1851, the first official text to contain this solution, applied the title *Liquor Arsenici Chloridi*. It was continued from this Pharmacopœia to the first British Pharmacopœia, of 1864, under title *Liquor Arsenici Hydrochloricus*, this title continuing up to the last revision.

The U. S. Pharmacopœia of 1870 introduced this solution under the title of *Liquor Arsenici Chloridi*, but changed it to *Liquor Acidi Arsenosi* in the 1880 revision, this title being also official in the last revision.



The change in title from *Liquor Arsenici Chloridi* to *Liquor Acidi Arsenosi* was evidently due to a better understanding of the chemistry of the solution. Duparquier<sup>1</sup> in 1841 explained the “increased solubility of arsenious acid in acidulated water” as being due to the formation of arsenous chloride, by the action of hydrochloric acid on the arsenic trioxide. This interpretation possibly led the revisors of both U. S. P. and B. P. to adopt the use of the above title. Stille and Maisch,<sup>2</sup> in 1879, called attention to the fact that arsenous chloride decomposed into arsenous acid and hydrochloric acid when dissolved in water, and state “the official solution contains therefore, simply the two acids.” Oldberg and Wall<sup>3</sup> in 1884 state that “The title of chloride of arsenic was erroneously given this preparation in the Pharmacopœia of 1870. It does not contain chloride of arsenic but is a solution of arsenous acid in water acidulated with hydrochloric acid.”

Wood and Bache<sup>4</sup> in 1886 state that “The hydrochloric acid does not enter in combination with the arsenous acid, it merely aids in its solution. The British title is in our opinion to be preferred, because the U. S. name does not indicate the presence of the hydrochloric acid.”

That the present title *Solution of Arsenous Acid* not only fails to indicate the presence of the hydrochloric acid, but also that it may be misleading as to the nature of the arsenic in solution, is quite evident. The revision committee for 1900 changed the title for  $\text{As}_2\text{O}_3$  from *Acidum Arsenosum* to *Arsenii Trioxidum*,

<sup>1</sup> *Jour. de Pharm.*, 27, p. 717 (1841).

<sup>2</sup> “National Dispensary,” 2 ed., p. 839 (1879).

<sup>3</sup> “Companion to the U. S. P.,” p. 184 (1884).

<sup>4</sup> “U. S. Dispensary,” 15th ed., p. 859 (1886).

the former title being regarded as a "misnomer."<sup>1</sup> If the hydrochloric acid does not react with the arsenic trioxide, the only explanation that might be offered as a reason for calling a solution of arsenic trioxide in water a solution of arsenous acid, is the hydration of  $As_2O_3$  to the acid of which it is the anhydride. Although a one per cent solution of arsenic trioxide in water shows an acid reaction to litmus and several other indicators, it is apparently neutral towards a greater number. (See table of indicators and tests paper No. 1.)

2. *Definition.* A definition appears for the first time in the 1900 revision. A slight modification of the purity rubric adopted by the 1910 revision was probably necessitated by the pure Food and Drugs Act of 1906 which demanded reasonable limits rather than an absolutely fixed standard.

3. *Form of Arsenic Trioxide Used.*—The U. S. P. of 1870 directs that the  $As_2O_3$  used should be in the form of "small pieces."<sup>2</sup> The editions of 1880 and 1890 simply specify "arsenous acid" and "arsenic trioxide" respectively,<sup>3</sup> and the 1910 edition directs "fine powder."

4. *Hydrochloric Acid as an Ingredient.*—This acid is used to facilitate the solution<sup>4</sup> of the arsenic trioxide in water. Two fluid drachms of "muriatic acid,"<sup>5</sup> equivalent to 42.6 grains HCl to 64 grains of arsenic trioxide were prescribed by the U. S. P. of 1870; two parts of "hydrochloric acid,"<sup>6</sup> equivalent to 0.638 parts of HCl, to one part of arsenic trioxide according to the U. S. P. 1880; fifty cubic centimeters of "diluted hydrochloric acid"<sup>7</sup> equivalent to 5.2 Gm. of HCl, to ten grams of arsenic trioxide according to the U. S. P. 1890; and according to the last two revisions fifty grams of "diluted hydrochloric acid," equivalent to 5 Gm. HCl, to ten grams of arsenic trioxide, was prescribed. The ratio of absolute hydrochloric acid and arsenic trioxide are herewith tabulated:

	HCl.	Arsenic Trioxide.
U. S. P. 1870	42.6 grains	64 grains
U. S. P. 1880	0.638 part	1 part
U. S. P. 1890	5.2 grams	10 grams
U. S. P. 1900	5.0 grams	10 grams
U. S. P. 1910	5.0 grams	10 grams

<sup>1</sup> "Proc. of the Pharmacopœial Convention," 1900, *Cir.*, 269, p. 1100.

<sup>2</sup> The explanation for this is found in the following statement made by the editors of the U. S. Dispensary, 13th ed. (1872), p. 1267: "In making this preparation (Fowler's Solution) care should be taken that the arsenious acid be pure. This object is best secured by using the acid in small pieces instead of powder. Sulphate of lime is a common impurity in the powdered acid, and if present will remain undissolved, and cause the solution to be weaker than it should be." Although the U. S. P. of 1870 directs a qualitative test (complete volatilization) to be made, that would bar such impurity as sulphate of lime, the U. S. P. of 1880 is the first to direct the assay of "Arsenious acid."

<sup>3</sup> The description for arsenic trioxide in these two editions reads "A heavy solid occurring either as an opaque white powder or irregular masses of two varieties. . . ."

<sup>4</sup> "U. S. Dispensary," 15th ed., p. 859.

<sup>5</sup> "An aqueous solution of hydrochloric acid gas of the specific gravity 1.160," U. S. P.

<sup>6</sup> "A liquid composed of 31.9 per cent of absolute hydrochloric acid (. . . .) and 68.1 per cent of water. Specific gr. 1.160," U. S. P. 1880.

<sup>7</sup> "Should contain 10 per cent of absolute hydrochloric acid." U. S. P. 1890 and 1900. "Not less than 9.5 per cent, nor more than 10.5 per cent of HCl," U. S. P. 1910.

5. *Ratio of Ingredients.*—De Valangin in his formula used 30 grains of arsenous acid to 90 grains of hydrochloric acid for 20 fluid ounces of the solution. The same ratio of ingredients existed in the London Pharmacopœia of 1851. The British Pharmacopœia of 1864, probably for the sake of uniformity, increased the arsenic content to that of Fowler's Solution, *viz.*, 80 grains to the Imperial pint; the 1885 revision increased the amount of arsenous acid to 87 grains, the amount of hydrochloric acid being 2 f. drachms for both revisions. The 1914 revision of the British Pharmacopœia prescribes 10 grams of "arsenous anhydride" to 12 mils of hydrochloric acid in 1000 mils of the solution. The ratio of arsenic trioxide to absolute hydrochloric acid for the several revisions is as follows:

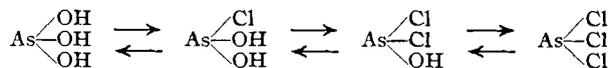
U. S. P.	Arsenic Trioxide.	HCl.	Vol. of product.
1870	1.0	0.69	119 cc.
1880	1.0	0.638	100 cc.
1890	1.0	0.525	100 cc.
1900	1.0	0.50	100 Gm.
1910	1.0	0.50	100 Gm.

6. *Water.*—De Valangin in his original formula directed the use of distilled water. Both British (also London) and United States Pharmacopœias used distilled water throughout.

7. *Amount of Water Used to Effect Solution.*—De Valangin directed the use of one fluid ounce of water to effect the solution of his "solvent mineral" with the aid of the hydrochloric acid, as did also the London Pharmacopœia of 1851. The British Pharmacopœia of 1864 increased the quantity to four ounces, having at the same time increased the amount of arsenic trioxide from 30 grains to 80 grains. The next change was made in the 1914 revision where 500 millilitres of water are directed to be used to dissolve 10 grams of arsenic trioxide.

In every edition of the U. S. Pharmacopœia, the amount of water used to effect the solution of the arsenic trioxide and hydrochloric acid represents one-fourth of the total volume prepared.

8. *Solution of Arsenic Trioxide.*—As already pointed out, the chemistry of the reaction mixture of  $\text{As}_2\text{O}_3$ ,  $\text{H}_2\text{O}$  and  $\text{HCl}$  may be regarded from the viewpoint of the hydration of the arsenic trioxide (for details see paper No. 1) and subsequent action of the  $\text{HCl}$  on the ortho arsenous acid. On the other hand it is well known that the reverse reaction does take place when water is added to arsenic trichloride. Hence the reactions as suggested by the following formulas are reversible, as indicated by the directions of the arrows.

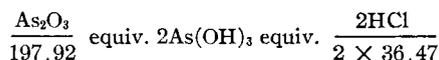


At what point the equilibrium is reached for the system indicated by the U. S. P. formula for *Liquor Acidi Arsenosi*, is not known. The contrasting conceptions held with regard to the chemistry of this solution are indicated by the several names applied thereto, as shown under Synonyms. The possibility of an equilibrium without committance to any formula or formulas is suggested—though possibly not intended—by the B. P. title *Liquor Arseni Hydrochloricus*.

Two simple means suggested themselves for a purely chemical study of this phase of this liquor. The first, to ascertain how hydrogen chloride facilitates the solution of arsenic trioxide in water. The second, to ascertain what action water would have on arsenic trichloride dissolved in an indifferent solvent which at the same time was insoluble in water.

A. *Hydrogen Chloride as an Aid to Dissolving Arsenic Trioxide in Water.*—This problem was attacked upon the basis of the following theoretical considerations. In order to be able to work under ordinary conditions of pressure, the strength of the hydrochloric acid not greater than the octahydrate was chosen. For 100 mls of reaction mixture this would admit 20.2 Gm. of HCl to 10 Gm. of  $\text{As}_2\text{O}_3$  taken for each experiment. This amount of  $\text{As}_2\text{O}_3$  was chosen because of the rate of solubility of arsenous acid anhydride in hot and cold water respectively. 1.6 Gm. of  $\text{As}_2\text{O}_3$  are said to be soluble in water to make 100 mls at 15 degrees centigrade. Its solubility in boiling water is recorded as being 6 Gm. in 100 mls. Hence a solution of 10 grams of arsenic trioxide in 100 mls of liquid must have been effected with the aid of the HCl. Inasmuch as the increase in volume of the solution due to the 10 Gm. of  $\text{As}_2\text{O}_3$  was not considered as a factor of appreciable importance in this case, the amount of diluted hydrochloric acid used was always 100 mls merely as a matter of convenience. No attempt was made to attain absolute accuracy.

In order to be in a position to choose molecular ratios so far as possible, the amounts of HCl taken were based upon the following equivalents representing the action of one molecule of hydrogen chloride on one molecule of ortho arsenous acid,



Hence 10 grams of  $\text{As}_2\text{O}_3$  would require 3.66 grams of HCl to change theoretically the hydrated  $\text{As}_2\text{O}_3$  or  $\text{As(OH)}_3$  to the monochloride dihydroxide,  $\text{As(OH)}_2\text{Cl}$ . Therefore the maximum number of molecules of HCl available with a hydrochloric acid not stronger than the octahydrate would be about 5.5 molecules. This would admit of a theoretical conversion of all of the  $\text{As(OH)}_3$  to  $\text{AsCl}_3$  and an excess of 2.5 molecules to prevent complete reversal of the reaction because of the solvent, water.

The experiments were carried out by adding 10 grams of arsenic trioxide to 100 mls of boiling water containing the required amount of hydrochloric acid representing one, two and three, etc., molecules of HCl, and immersing the mixture in a bath of boiling water until a clear solution resulted. The mixture was continually agitated and the time required to effect a clear solution recorded. The first concentration from which a clear solution was obtained was that representing  $\frac{\text{As}_2\text{O}_3}{2}$  to 4HCl in 100 mls. Weaker acid concentrations gave no solution after one hour of heating. The results are herewith tabulated:

$\text{As}_2\text{O}_3$ , Gm.	HCl, Gm.	Vol. of sol.	Time (min.)	Ratio.
10	12.8	100 mls	no. sol.	$\frac{\text{As}_2\text{O}_3}{2}$ to $3\frac{1}{2}$ HCl
10	14.68	100 mls	12, 10, 10	$\frac{\text{As}_2\text{O}_3}{2}$ to 4 HCl
10	16.5	100 mls	6, 6	$\frac{\text{As}_2\text{O}_3}{2}$ to $4\frac{1}{2}$ HCl

As <sub>2</sub> O <sub>3</sub> , Gm.	HCl, Gm.	Vol. of sol.	Time (min.)	Ratio.
10	18.35	100 mils	3, 3	$\frac{\text{As}_2\text{O}_3}{2}$ to 5 HCl
10	20.18	100 mils	2, 2	$\frac{\text{As}_2\text{O}_3}{2}$ to 5½ HCl

Upon cooling the solution, crystals, apparently octahedric in shape, were deposited. According to H. Rose, "A solution of 2 or 3 parts of amorphous As<sub>4</sub>O<sub>6</sub> in 12 parts of concentrated HCl aq. deposits crystals of the octahedral oxide when slowly cooled." (From "Watts Chemical Dictionary," v. 1, p. 312, 1890. Taken from Poggendorf's *Annal. d. Physik. u. Chem.* 35, p. 481.)

That the hydrochloric acid aids in the solution of the arsenic trioxide can readily be concluded. Furthermore, the increased solubility of arsenic trioxide in water (see table) in the presence of hydrochloric acid would seem to indicate that a reaction had taken place between the hydrogen chloride and the arsenic trioxide. The fact that the arsenic trioxide crystallizes out from such a solution indicated that this reaction is not a quantitative one in the direction of the simple equation, but that its solution is a multiple phase solution.

In the comparison of the equivalent ratios with the ingredient ratios of the U. S. P. formula the following computations have proven helpful:

$\begin{array}{l} \text{As}-\text{Cl} \\ \quad \diagdown \\ \quad \text{O} \\ \quad \diagup \\ \text{As}-\text{OH} \end{array}$	$\frac{\text{As}_2\text{O}_3}{1} + \text{HCl}$ <p style="text-align: center;">1 to 0.1842</p>	$\frac{\text{As}_2\text{O}_3}{2} + 3\frac{1}{2}\text{HCl}$ <p style="text-align: center;">1 to 1.28</p>
$\begin{array}{l} \text{As}-\text{Cl} \\ \quad \diagdown \\ \quad \text{O} \\ \quad \diagup \\ \text{As}-\text{Cl} \end{array}$	$\frac{\text{As}_2\text{O}_3}{1} + 2\text{HCl}$ <p style="text-align: center;">1 to 0.367</p>	$\frac{\text{As}_2\text{O}_3}{2} + 4\text{HCl}$ <p style="text-align: center;">1 to 1.46</p>
$\begin{array}{l} \text{As}-\text{Cl} \\ \quad \diagdown \\ \quad \text{OH} \\ \quad \diagup \\ \quad \text{OH} \end{array}$	$\frac{\text{As}_2\text{O}_3}{2} + \text{HCl}$ <p style="text-align: center;">1 to 0.367</p>	$\frac{\text{As}_2\text{O}_3}{2} + 4\frac{1}{2}\text{HCl}$ <p style="text-align: center;">1 to 1.651</p>
$\begin{array}{l} \text{As}-\text{Cl} \\ \quad \diagdown \\ \quad \text{Cl} \\ \quad \diagup \\ \quad \text{OH} \end{array}$	$\frac{\text{As}_2\text{O}_3}{2} + 2\text{HCl}$ <p style="text-align: center;">1 to 0.734</p>	$\frac{\text{As}_2\text{O}_3}{2} + 5\frac{1}{2}\text{HCl}$ <p style="text-align: center;">1 to 1.835</p>
$\begin{array}{l} \text{As}-\text{Cl} \\ \quad \diagdown \\ \quad \text{Cl} \\ \quad \diagup \\ \quad \text{Cl} \end{array}$	$\frac{\text{As}_2\text{O}_3}{2} + 3\text{HCl}$ <p style="text-align: center;">1 to 1.10</p>	$\frac{\text{As}_2\text{O}_3}{2} + 6\text{HCl}$ <p style="text-align: center;">1 to 2.202</p>

9. *Volume of Finished Product.*—De Valangin originally prepared twenty fluid ounces, the Imperial pint. Likewise did the London Pharmacopœia of 1851, and the subsequent editions of the British Pharmacopœia. The 1914 edition of the British Pharmacopœia having wholly adopted the metric system, brings the volume of the finished product up to 1000 mils. According to the U. S. P. of 1870, the finished product was diluted to "exactly one pint." In 1880 "up to 100 parts;" in 1890 "up to 1000 cc.," and in the last two revisions each "up to 1000 grams."

The ratio of arsenic trioxide to finished product is approximately as follows:

	Arsenic trioxide.	Product.
De Valangin's Sol.	0.345 Gm.	to 100 mils
Ph. London 1851	0.345 Gm.	to 100 mils
B. P. 1864 and 1867	0.915 Gm.	to 100 mils
B. P. 1885, 95, 1914	1.0 Gm.	to 100 mils

U. S. P. 1870	0.84 Gm. to 100 mils
U. S. P. 1880, 1890	1.0 Gm. to 100 mils
U. S. P. 1900, 1910	1.0 Gm. to 100 grams

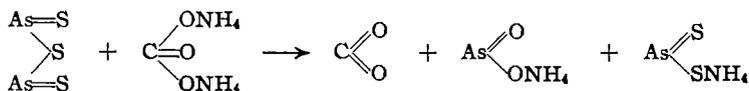
It becomes apparent that in order to make this solution correspond in strength to Fowler's solution the ratio of arsenic trioxide to finished product was increased considerably over that of De Valangin's original formula, and also that of the London Pharmacopœia.

10. *The Appearance of the Finished Product.*—The U. S. P. of 1880 and the editions following direct that the solution be filtered. No mention of filtering is made in the revision of 1870.

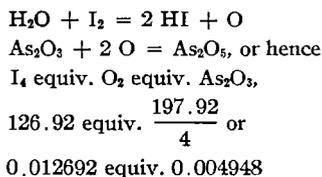
11. *Qualitative Tests.*—The U. S. P. of 1890 is the first one to contain a qualitative test and this only a descriptive one. Likewise the 1900 revision contains but this test. The last edition, that of 1910, gives one additional test. The first is a descriptive statement; the second a test for arsenic. The acid reaction of the solution described in the first test may be attributed to the hydrochloric acid present, also due to the hydrolysis of the arsenic trioxide. (See No. 8.) The second test: upon saturating the solution with hydrogen sulphide a yellow precipitate of arsenous sulphide is formed. This precipitate is soluble in Ammonium Carbonate T. S. The reaction with ammonium carbonate has been indicated as follows:<sup>1</sup>



Structurally the formulas involved may be represented in the following manner:



12. *Assay.*—From 1880 on the U. S. P. gives directions for the assay of this solution. The quantitative determination of trivalent arsenic as  $\text{As}_2\text{O}_3$  is not only a check on the amount of arsenic trioxide employed, but also on the possible deterioration of the solution, brought about by the oxidation of the arsenous to arsenic, in the presence of water, as expressed by the following reactions:



The amount of  $\text{As}_2\text{O}_3$  as determined by the prescribed volumetric assay varies to a slight degree. The U. S. P. of 1880, the first to introduce an assay method, states that 24.7 Gm. of the solution "should require from 48.5 to 50 cc. of volumetric solution of iodine"—("corresponding to 1 per cent of arsenious acid of the required purity"). The  $\text{As}_2\text{O}_3$  equivalents of 48.5 and 50 cc., respectively, of *N*/10 I. V. S. are 0.9709 Gm. and 1.001 Gm. As the purity rubric for "arsenious acid" was "at least 97 per cent pure," ten grams, the amount directed to be used to make

<sup>1</sup> "Commentar zur Pharmacopœia Helvetica" (1896) p. 196.

1000 cc. of the Liquor, would represent 0.9700 gram  $\text{As}_2\text{O}_3$  to 100 cc. of the solution. Hence, unless the "arsenious acid" used assayed slightly higher than the minimum U. S. P. requirement, the finished product would fall short by a very slight amount (within the limits of experimental error) of the given standard.

The U. S. P. of 1890 states that 24.7 cc. of the solution "should require from 49.4 to 50 cc. of decinormal iodine V. S."—"corresponding to 1 Gm. of arsenous acid in 100 cc. of the solution"). The  $\text{As}_2\text{O}_3$  equivalents of 49.4 cc. and 50 cc. *N*/10 I. V. S. according to this revision represent 0.9883 Gm. and 1.004 Gm. respectively of  $\text{As}_2\text{O}_3$  in 100 cc. of the solution. As the purity rubric for "arsenous acid" in this revision is "at least 98.8 per cent of arsenic trioxide," ten grams, the amount prescribed to make 1000 cc. of the Liquor, would represent 0.988 Gm. to 100 cc. of the solution. In this case the minimum requirement would be met.

The U. S. P. of 1900 states that 24.6 Gm. of the solution "should require not less than 50 cc. of tenth-normal iodine V. S.—" ("corresponding to 1 Gm. of arsenic trioxide in 100 Gm. of the solution"). The  $\text{As}_2\text{O}_3$  equivalent of 50 cc. of *N*/10 I. V. S. according to this revision represents 0.9981 Gm. of  $\text{As}_2\text{O}_3$  in 100 Gm. of the solution. The new purity rubric for arsenic trioxide is "not less than 99.8 per cent of pure Arsenic Trioxide." Hence ten grams of arsenic trioxide, as directed to be used for the preparation of 1000 grams of the Liquor, would represent only 0.998 Gm. of  $\text{As}_2\text{O}_3$  to 100 Gm. of the solution. In this instance the conditions meet the requirement of 10 Gm. of arsenic trioxide, which represents 9.98 Gm. of  $\text{As}_2\text{O}_3$ .

The U. S. P. of 1910 merely demands a definite percentage strength, *viz.*, "not less than 0.975 nor more than 1.025 Gm.  $\text{As}_2\text{O}_3$  in 100 Gm. of the solution," and makes no mention of the amounts of *N*/10 I. V. S. to be used. The purity rubric for arsenic trioxide for this revision is "not less than 99.8 per cent. of  $\text{As}_2\text{O}_3$ ." It is quite evident, however, that the maximum limit of  $\text{As}_2\text{O}_3$  content of the solution will probably not result when the prescribed ten grams of arsenic trioxide are used, as this represents only 0.998 Gm. of  $\text{As}_2\text{O}_3$  to 100 Gm. of the solution. The lower limit of the rubric, *viz.*, 0.975 Gm. to 100 Gm. of solution, is undoubtedly to allow for a slight loss of arsenic trioxide, as determined by the assay process, due to the oxidation of the trivalent-arsenic to the pentavalent arsenic.

Two factors influence the variations mentioned above: firstly, the variation in the  $\text{As}_2\text{O}_3$  equivalent of *N*/10 I. V. S. due to changes in atomic weights, and secondly, the purity rubric of the arsenic trioxide. The cc. equivalent for 1880 was 0.004945; for 1890, 0.004942; for 1900, 0.004911; and for 1910 it is 0.004948. The purity rubric for arsenic trioxide for 1880 was 97 p. c.  $\text{As}_2\text{O}_3$ ; for 1890, 98.8 p. c.  $\text{As}_2\text{O}_3$ ; for 1900, 99.8 p. c.  $\text{As}_2\text{O}_3$  and for 1910 it is 99.8 p. c.  $\text{As}_2\text{O}_3$ .

Inasmuch as only one gram of arsenic trioxide is used to prepare 100 grams of the solution, it becomes quite apparent that any solution assaying 1 p. c.  $\text{As}_2\text{O}_3$  (the generally accepted U. S. P. requirement) would result only from carelessness in weighing, unless it be that the U. S. P. formula were ignored and the equivalent of 10 Gm. of 100 p. c. pure arsenic trioxide were used, or that a 100 p. c. arsenic trioxide were used.

13. *Dose*.—A dose is first prescribed by the U. S. P. 1900. This is designated as, "Average dose—0.2 cc. (3 minims)." The revision of 1910 likewise contains the dose given as, "Average dose—metric, 0.2 mil.—Apothecaries, 3 minims." This

corresponds with the dose of arsenic trioxide, *viz.*, 0.002 Gm. or  $\frac{1}{33}$  grain. (For history of introduction of doses in U. S. P. see paper No. 1.)

(To be continued)

## TEACHING THE USE OF THE MORTAR.

BY R. A. BAKER.\*

In teaching the principle of grinding successive small portions of material rather than a single large portion, the following test has been found to be very efficient with a class of several hundred in freshman chemistry.

After a lecture demonstration and discussion of the proper method, each student is given in the laboratory an envelope containing 10 grams of cracked gypsum, previously freed from dust on a 20-mesh sieve. On the outside of this envelope he enters his name, the name of his laboratory instructor and the internal diameter of his mortar. This measurement is checked and initialed by his instructor. The class is then told that but two minutes will be allowed for grinding this gypsum and that the grade which each student receives on the exercise will depend upon the amount which he grinds fine enough to pass through a 60-mesh sieve. Beyond this the student is left to his own devices. At a given signal the grinding begins and at the end of the two-minute period a whistle (necessarily a loud one) announces that all grinding must stop. Each student then returns to the original envelope all material, ground and unground, and hands it to his instructor.

The grades are determined by actually sifting and weighing each sample. We have employed student help for this purpose, and are convinced that the expense is fully justified. The net cost to the department can be cut down by having the students grind some material, such as gypsum, for which there will be a demand later in the course. It is not necessary to make a quantitative separation of the powder for, if every sample receives the same treatment, the results will stand in the same relative order, which is the chief requirement in estimating the student's mark or grade.

In lieu of a mechanical shaker one can save considerable time by carefully following a few arbitrary rules to insure uniformity. (1) Use the same sieve for all samples. (2) Tap it sharply the same number of times after each sifting, first right-side-up and then up-side-down. (3) Use the same general motion. (4) Shake for 30 seconds only. (5) Have in the sieve one or more coins to aid in scattering the material. (Samples of gypsum, sifted in accordance with these rules, showed a 95% separation of the 60-mesh powder actually present.)

Over 1000 students, about half of them women, have already taken this test. The results have been analyzed in order to determine what allowance must be made for the size of the mortar and whether the same results could be expected from the women as from the men. This analysis appears in the following table:

Weight of material.	Diameter of mortar.	Duration of grinding.	Weight of 60-mesh powder.	Extremes.
Men 10 Gm.	5 cm.	2 minutes	5.00 Gm.	1-10 Gm.
Men 10 Gm.	10 cm.	2 minutes	7.98 Gm.	2-10 Gm.
Women 10 Gm.	5 cm.	2 minutes	4.36 Gm.	2- 8 Gm.
Women 10 Gm.	10 cm.	2 minutes	6.46 Gm.	3-10 Gm.

\* Professor of Inorganic Chemistry, Syracuse University.