

**BULLETIN OF THE UNIVERSITY OF
WISCONSIN, SERIAL NO. 1153. GENERAL
SERIES NO. 936. A CENTURY OF THE
UNITED STATES PHARMACOPOEIA,
1820-1920; LIQUOR POTASSII ARSENETIS**

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H. A. LANGENHAN

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A CENTURY OF THE UNITED STATES
PHARMACOPOEIA, 1820-1920

LIQUOR POTASSII ARSENETIS

BY

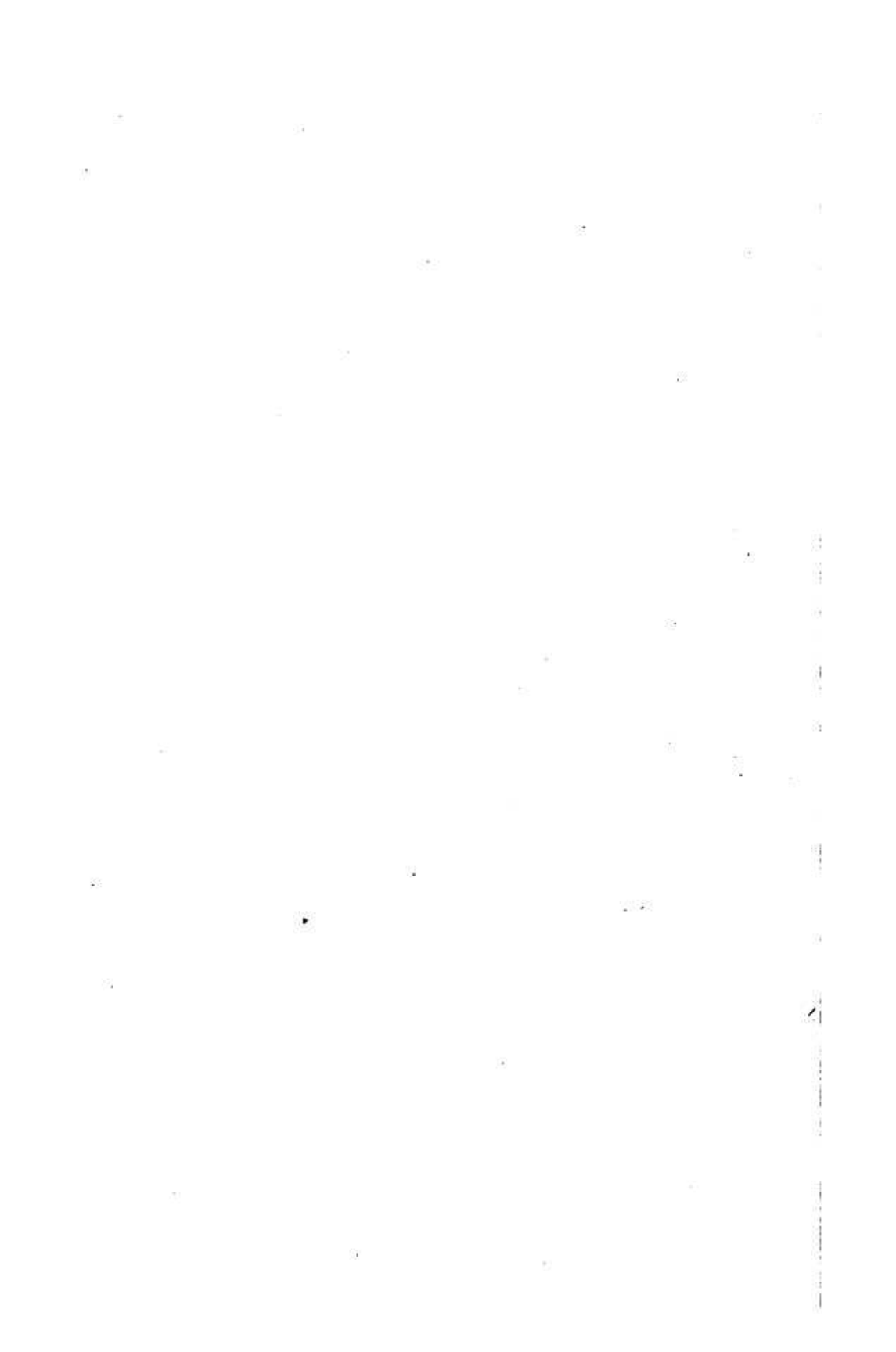
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TABLE OF CONTENTS.

	Page
INTRODUCTORY STATEMENT.	
History of Arsenic Therapy.....	1
Arsenical Preparations of the U. S. P. and N. F.....	2
SOLUTION OF ARSENOUS ACID AND ITS SALTS.	
Introductory Statement	3
Hydration of As_2O_3	3
Action of Alkalies on Arsenous Acid.....	5
Action of Hydrogen Chloride on Arsenous Acid.....	6
LIQUOR POTASSII ARSENITIS (Fowler's Solution).	
History and Original Formula.....	6
Names and Synonyms including Pharmacopoeial Synonymy..	9
Text of the U. S. P. 1820 to 1920 and Comments.	
Introductory Remarks	13
Text	14
Comments.	
1.) Title and Synonyms	20
2.) Definition	20
3.) Preservation	20
4.) Arsenic Trioxide as an Ingredient.....	23
5.) The Form in which it is used.....	23
6.) Potassium Carbonate or Bicarbonate as an ingredient	24
7.) Ratio of Ingredients	24
8.) Water	25
9.) Amount of water used to effect solution.....	25
10.) Solution of Arsenic Trioxide.....	28
11.) Alcohol and Compound Tincture of Lavender...	37
12.) Volume of finished Product.....	38
13.) Appearance of finished Product.....	40
14.) Qualitative tests	40
15.) Assay	43
16.) Dose	45
Appendix.	
English Patents	47
Wilson's Patent	48
Fowler's Report	49

INTRODUCTORY STATEMENT

The history of arsenic therapy is of considerable interest in the evolution of the *materia pharmaceutica*. Natural compounds of arsenic, such as realgar and auripigment were used during antiquity,¹ but primarily for external purposes. Because of the change which they produced in the color of copper, arsenical compounds have played an important role during the alchemistic period of chemical history.² As a result, new derivatives of arsenic were discovered,³ some of which at least were destined to play a role in the battles between the iatrochemists and the representatives of the old or Galenic School of Medicine.⁴ A larger increase to the number of arsenic compounds, however, did not come until the close of the eighteenth and the beginning of the nineteenth cen-

¹ For a concise statement of the knowledge of the ancients, see Kopp, *Geschichte der Chemie*, vol. 4, p. 89.

Berendes, *Des Pedantos Dioskurides Arzneimittellehre*, p. 531 (Chap. 120: Arsenikon; and Chap. 121: Sandaracha.)

Pliny, *Natural History* (Bohn's Classical Library, vol. 6, p. 104 (Orpiment) and p. 220 (Sandarach and Arrhenicum).

Scribonius Largus (Felix Rinne, *Das Receptbuch des Scribonius Largus*, vol. 5 of R. Kobert, *Historische Studien aus dem Pharmakologischen Institute der k. Universität Dorpat*, p. 79 (Auripigmentum) and p. 84 (Sandaraca.)

For a more detailed account see, "Historical Notes on Arsenic and its principal combinations: by G. F. Babcock, *New Remedies*, vol. 12, (1883) pp. 98, 151 and 170.

² Comp. E. v. Meyer, *History of Chemistry* (3rd ed.) p. 58: "On account of this behaviour, the pseudo-Geber calls arsenic *Medicina Venerea dealbans*". See also Kopp, *Geschichte der Chemie*, vol. 4, p. 94.

³ The *arsenicum album* (As₂O₃) of the alchemists; the *arsenicum fixum* of Paracelsus (arsenic acid or its potassium salt). Kopp, *Geschichte der Chemie*, vol. 4, p. 95.

⁴ Meyer, *History of Chemistry* (3d ed.) p. 94.

ture.⁵ Still later followed the organic derivatives of arsenic that formed the basis of the classical researches by Bunsen.⁶ Comparatively few of these have found application in medicine, one of the latest being the much discussed specific "606" or *salvarsan*.⁷

If the chemotherapy of arsenic includes but few of its compounds, pharmacopoeial preparations of the derivatives of this element are even less numerous. Those of the U. S. P. and N. F. are but seven in number and can be grouped as follows:

- 1.) Solutions of arsenous acid and its salts:
 - 1.) *Liquor Acidi Arsenosi*, U. S. P.
 - 2.) *Liquor Potassii Arsenitis*, U. S. P.
- 2.) Solutions of arsenates:
 - 3.) *Liquor Sodii Arsenatis*, U. S. P.
 - 4.) *Liquor Sodii Arsenatis*, Pearson, N. F.
 - 5.) *Liquor Arsenicalis*, Clemen's, N. F.
- 3.) Solutions of arsenic trihalides (or rather "double salts"):
 - 6.) *Liquor Arseni et Hydrargyri Iodidi*, U. S. P.
 - 7.) *Liquor Auri et Arseni Bromidi*, N. F.

I. SOLUTIONS OF ARSENOUS ACID AND ITS SALTS.

The so-called "arsenious acid" of the older chemists, our arsenous acid anhydride, or arsenic trioxide, is but sparingly soluble in water, yet sufficiently soluble to form solutions with a 1 p. c. As_2O_3 content. Nevertheless such a solution is not official in any of the latest editions of the pharmacopoeias.⁸ Neither does the simple solution appear to be prescribed at present by physicians, although arsenic trioxide is frequently prescribed in solid form as pill,⁹

⁵ Kopp Geschichte der Chemie, 4, p. 96.

⁶ The reprint of these has been edited by A. v. Baeyer in Ostwald's Klassiker der exakten Wissenschaften, vol. 27.

⁷ This epoch making discovery is discussed by Schweizer "Ehrlich's Chemotherapy—a new science" in Science, vol. 32, p. 809. (Dec. 9, 1910.)

⁸ In the French Codex of 1884 a *Solutio Arsenical ou Minéral* (Boudin), one-tenth as strong as the corresponding U. S. P. arsenical solution, was official, but has been dropped in the latest edition. See also Dorvault, *L'Officine*, 15th edition (1910), p. 1289, which also gives a formula for a *Solutio Arsenical* (Isnard), which is only one-tenth of the strength of Boudin's solution.

⁹ Arsenic trioxide enters the *Pilule Ferræ, Quininae, Strychninae et Arseni fortiores* of the National Formulary 4th revision; also *Pilule F. Q. S. et As. mites*, N. F. IV with less arsenic trioxide.

The French Codex of 1866 and 1884, but not the latest edition, contains *Granules d'Acide Arsenique*; also *Pilules Arsenicales (Pilules Astatiques)*; see also, *L'Officine* 15th edition (1910), p. 1061; Blax, *Lectures on Pharmacology*, vol. 2, (1897), p. 88, translation by Latham.

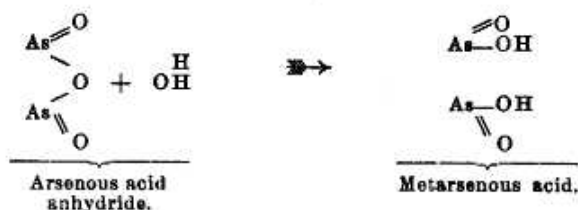
powder,¹⁰ or tablet. The slow solubility of arsenic trioxide in water may be accelerated either by hydrochloric acid or by potassium carbonate. The question may well arise, are these adjuncts mere pharmaceutical conveniences or do the resulting reaction mixtures differ sufficiently chemically to make the products different therapeutic agents? If essentially alike as therapeutic agents, another pharmaceutical question may be asked, viz., are the two solutions required in medical practice to avoid chemical incompatibilities when prescribed with other substances? The first question is answered in the negative by modern pharmacologists.¹¹ The so-called neutral solution being unstable,¹² the acid and alkaline solutions afford pharmaceutical advantages only. Both are official so that incompatibilities may be avoided by using either the one or the other.¹³

In a general way, the chemistry of these two solutions has certain aspects in common, hence may be considered together if for no other reasons than to avoid unnecessary repetition. The reactions involved may be reviewed from the following points of view:

- A.) The hydration of arsenic trioxide.
- B.) The action of an alkali, such as potassium hydroxide or potassium carbonate, on the hydration products.
- C.) The action of hydrogen chloride on the hydration products.

A. Hydration of arsenic trioxide.

When arsenic trioxide, arsenous acid anhydride, is dissolved in water, its hydration to metarsenous and other arsenous acids may be assumed. This hydration finds a ready expression in the following structural formulas of these compounds:¹⁴



¹⁰ In the French Codex of 1866 there was official a *Poudre d' Acide Arsenieux*.

¹¹ See letters by Bernard Fantus, A. S. Loevenhart, and Torald Sollmann.

¹² See letter by Dr. Withering, in Fowler's Report, p. 124.

¹³ See letters by Dr. Fantus and Dr. Sollmann.

¹⁴ Similar formulas are used by A. Stavenhagen in his article on "Beitrag zur Kenntniss der Arsenite". Journ. pr. Chem. (1895) 169, p. 1.