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CHEMICAL MONOGRAPHS AND NEW CHEMICALS IN U. S. P. IX.*

BY OTTO RAUBENHEIMER.

One of the principal features of the new Pharmacopoeia is the addition of 34 chemicals. More would have been added, especially of the newer chemicals, were it not for the general principle followed in the Revision that "No substance shall be introduced if controlled by patent rights." Nevertheless, the Sub-Committee on Scope recommended the addition of several patented or synthetic chemicals. When permission was asked from the manufacturers to include these chemicals in U. S. P., this was in most cases refused. A sure proof that manufacturers are not overanxious to officialize their products, or do not care to enlighten pharmacist or physician. I became fully convinced of this after a conversation with an agent of a manufacturer, who openly told me that he wanted physicians to remember the short, euphonious, therapeutic name of his product, but not the long chemical term! Truly not the right kind of spirit in our enlightened, but commercial age!

* Read before Scientific Section, A. Ph. A., Atlantic City meeting, 1916.

The admissions, as well as the deletions, have been governed by 2 basic principles formulated by the Sub-Committee on Scope under the chairmanship of Dr. S. Solis Cohen, namely "therapeutic usefulness and pharmaceutic necessity."

Before taking up the added chemicals, I will endeavor to analyze the most excellent arrangement of the chemical monographs in U. S. P. IX, for which the Sub-Committee on Inorganic and Organic Chemicals and the Editor, Prof. Remington, are responsible.

ARRANGEMENT OF CHEMICAL MONOGRAPHS.

The heading comprises 3 lines, namely the Latin title in large capitals, the English title, and in the third line the official abbreviation in solid block type, followed by one or more synonyms. The former are an innovation in pharmacopoeia making and will be found very useful by physicians in writing prescriptions and by pharmacists and chemists in labeling shop bottles. The abbreviations in common use have been adopted, as for instance, sulph. = sulphate, chlor. = chloride. In order to avoid confusion, similar terms as "sulphide" or "chlorate" are *not* abbreviated. Synonyms are printed in small type and in some cases are put in quotation marks, which indicates that this name, although not scientifically correct, is largely used in commerce. It is of great importance to note that "Substances labeled with an official synonym must comply with the standards, tests, and requirements demanded for the official article." It is to be regretted that the old nomenclature of alkaloidal salts, as chloride and bromide, has been adopted as synonyms. The sooner these are forgotten, the better it will be!

The title is followed by the Definition including the Empiric Formula, the Structural Formula and the Molecular Weight. The empiric formulas are very empiric, the total of each element being given. This in the case of organic acids is confusing and a great disadvantage as the replaceable hydrogen is not stated.

One novel feature, which is apt to be overlooked by many, is the change in the positions of N and O, in the formulas of organic chemicals, O being now placed before N. This is a decided improvement and in accordance with modern chemical literature and also the *Deutsche Arzneibuch*. The ending NO_3 in alkaloids, which looks to many, especially students, like a nitrate, is now reversed into O_3N! The position of the elements in organic formulas in U. S. P. IX is C, H, O, N; Cl, Br, I, F; S, P.

Structural Formulas are given, besides the Empiric Formulas, when necessary to indicate structural characteristics. The position of the radicals are indicated by numbers. No Graphic Formulas are given. The Atomic Weights are based upon O = 16 and the 1915 Report of the International Committee has been adopted.

Following the definition is the Purity Rubric, which was first introduced into U. S. P. VIII, and which greatly helped to make this work world famous. The language used is: "Containing, when dried to constant weight (in desiccator or at a specified temperature), not less than percent." In some instances a minimum and maximum purity are given. Whenever a purity rubric is stated in the first paragraph then an assay is given in the last paragraph. The figures given in the Purity Rubric represent requirements that can be reasonably demanded in each instance.

A statement on the preservation of the chemical ends the first paragraph, as for instance: Preserve in well-closed containers, or bottles—in a cool place—protected from heat and light, etc. Delicate chemicals, such as alkaloids, are to be preserved in dark amber-colored vials protected from light.

A Caution Note is added, when necessary, as for instance under Trinitrophenol.

Thus far the monograph is in 12 point type and the remainder is in 8 point type, not because the descriptions, etc. are of less importance, but in order to save space. This is well to remember, because in legal cases arguments have been made, that inasmuch as the type was smaller, the subject treated must be of less importance!

The *Physical Description* of the chemicals in U. S. P. IX is divided into several short paragraphs as follows:

Appearance, color and taste.

Solubility in water, alcohol, glycerin, chloroform, ether and other solvents.

Color of Solution and Reaction to litmus.

Melting or Boiling Point and also Specific Gravity of liquids.

Methods for the determination of melting, boiling and congealing points are given in Part II.

Solubilities are not expressed in "parts" as in U. S. P. VIII, but in the following manner: "*1 Gm.*.....dissolves in.....*mils* of.....at.....° C."

Full particulars are given in Part II, where also the statement is made that "solubilities are not intended as physical constants in the strict sense of the term, but primarily as information required by physicians and pharmacists in connection with the preparation and dispensing of medicines."

The *Chemical Description* in the U. S. P. IX is divided into paragraphs as follows:

Tests of Identity.

In the case of salts these are given for Base and Acid.

Tests of Purity.

These tests are followed by the impurities, in parentheses. The terms "Absence of" or "Limit of" are no longer used. Tests for Arsenic and Heavy Metals are given by reference to General Tests in Part II, in order to avoid repetition and to save space. An important change has been made in the language of the chemical tests. The conditional form of previous Pharmacopoeias, as "If—Gm. be dissolved," has been changed, *as it should be in a legal standard*, to the imperative "Dissolve.....Gm."

Assay.

When a Purity Rubric is given than an Assay is provided. Important changes have been made, changes for the better, as these assays are not intended for "tyros." Two metals, Hg and Zn and their salts have an alternative assay, namely, the Electrolytic Determination, which is fully described in Part II.

Biological Assays are only obligatory for Cannabis and its preparations and Pituitary Solution.

Preparation or Preparations:

The official preparations into which the chemical enters as an *active ingredient*

are again appended as in U. S. P. VII. This should be very useful for the practicing physician and also to students of pharmacy and medicine.

The monographs end with a statement in 12 point type:

Average Dose in both Metric and Apothecaries System.

CLASSIFICATION OF CHEMICAL ADDITIONS.

1 Acid: Phenylcinchoninic Acid.

13 Alkaloids and Alkaloidal Salts, namely:

- 3 Morphine Derivatives: Ethylmorphine Hydrochloride, Diacetylmorphine and Hydrochloride.
- 3 Purine Bases or Salts: Caffeine Sodio-Benzoate, Theobromine Sodio-Salicylate and Theophylline.
- 1 Cocaine Derivative, Beta-Eucaine Hydrochloride.
- 3 Quinine Salts, Dihydrochloride, Tannate and Quinine and Urea Hydrochloride.
- 3 Other Alkaloidal Salts, Cotarnine Hydrochloride, Emetine Hydrochloride and Hydrastine Hydrochloride.

The following 14 salts have been admitted:

- 1 Bismuth Salt, namely the Betanaphtholate.
- 2 Calcium Salts, Glycerophosphate and Lactate.
- 1 Creosote Salt, the Carbonate.
- 1 Mercury Salt, Mercuric Salicylate.
- 1 Potassium Salt, Sulphurated Potassa.
- 7 Sodium Salts, Benzolsulphinide, Cacodylate, Cyanide, Glycerophosphate and its 50 percent Solution, Indigotindisulphonate, Perborate and the exsiccated Sulphite.
- 1 Uranium Salt, the Nitrate.

The following compressed gases have also become official:

2 Gases, Nitrogen Monoxide and Oxygen.

Besides this, the following 5 chemicals have been admitted into U. S. P. IX: Glucose, Paraformaldehyde, Phenolphthalein, and Trinitrophenol.

DEPARTMENT OF AGRICULTURE PROPOSED RULING FOR DANDELION ROOT AND DEFINITION FOR CRAMP BARK

DANDELION ROOT—Examination of samples from a recent importation of dandelion root disclosed the presence of about 40 percent of roots, the interior of which were badly discolored and did not show a porous pale yellow wood, as required by the United States Pharmacopoeia, IX, 1916. The appearance suggested that the material had been improperly dried. This fact was confirmed by microscopic examinations showing swollen brownish yellow masses indicating that the inulin masses had been partially hydrolyzed and caramelized. The department will recommend the exclusion from the United States of any importation of dandelion root which, upon examination, is found to contain more than 10 percent of discolored or improperly dried roots.

USE OF THE TERM "CRAMP BARK."—The Bureau considers that the term "cramp bark" applies only to *Viburnum opulus*, now official in the National Formulary, and consequently should not be used for barks from other sources or their preparations.