

Section on Pharmacopoeias and Formularies

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BICHLORIDE TABLETS OF THE GERMAN PHARMACOPOEIA.

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Mercury, that is the metal, was already known in the time of the great Greek philosopher, Aristotle (384-322 B. C.), and held the highest place in the mediæval literature. Native mercury was found in the mines of Spain in liquid form and was therefore called *Argentum Vivum*, that is, living silver, or quicksilver. Chemistry, medicine and pharmacy are indebted to the Arabian alchemist, Abu-Musa-Dschafir-Ali-Sofi, commonly called Geber, which is the equivalent of his middle name, who discovered bichloride of mercury about the year 800. This he prepared by the sublimation of mercury, iron vitriol, alum, salt and saltpeter. The German chemist, Johann Kunkel, in 1716 greatly improved this process, which is still in use today, by subliming a mixture of mercuric sulphate and sodium chloride. It was Sir Humphry Davy, in 1810, who determined the chemical composition of corrosive sublimate as mercuric chloride. It is an everlasting credit to Paracelsus (1493-1541), the founder of iatro-chemistry or medical chemistry, to have introduced the mercurials into medicine as a specific against syphilis. Corrosive sublimate became a recognized cure for syphilis at the Vienna School of Medicine. It was there introduced by the celebrated Gerard van Swieten (1700-1772), the Dutch physician and pupil of the immortal Boerhaave. Van Swieten's solution of corrosive sublimate still holds its place in medicine and pharmacy.

The chemical and pharmaceutical industry in the United States most certainly deserves credit for the introduction as well as the evolution of tablet manufacture. Dr. Charles Meigs Wilson, of Philadelphia, in 1884 was the first to suggest the use of tablets of corrosive sublimate, which most decidedly have a great advantage in the extemporaneous preparation of solutions. The tablets suggested by him contain 7.7 grains of corrosive sublimate and 7.3 grains of ammonium chloride, each of which when added to a pint of water will make a solution of 1 in 1000. The addition of ammonium chloride serves three purposes, namely, it prevents the decomposition of the mercuric chloride, it hastens its solubility and produces a permanent solution. Since then these tablets have come into tremendous use.

In 1887, Dr. Angerer, professor of surgery at the University of Munich, and physician to the Bavarian court, recommended tablets composed of equal parts

of mercury bichloride and sodium chloride. These were introduced into the German Pharmacopoeia under the title

“*Pastilli Hydrargyri Bichlorati*” or “*Sublimatpastillen*.”

The following is a translation of the monograph of the 5th edition of the German Pharmacopoeia, 1910:

Content about 50 percent of mercuric chloride (HgCl_2 , molecular weight 270.9).

Equal parts of finely powdered mercuric chloride and sodium chloride are well triturated, the mixture is colored red with an aniline dye and is formed into tablets of a cylindrical shape, which are twice as long as thick and which should weigh either one or two grams.

Hard cylindrical pastilles of a red color, easily soluble in water but only partly soluble in alcohol and ether. The aqueous solution should not redden blue litmus paper.

Sublimate pastilles must be dispensed in well closed glass bottles, which must bear a poison label. Each tablet must be wrapped separately with black paper, which in white ink must bear the word “Poison,” as well as the amount of corrosive sublimate.

Must be kept preserved from light and moisture.

Must be kept in the poison closet under lock and key.

The fifth edition of the Deutsche Arzneibuch, 1910, also contains an assay for the determination of the mercuric chloride in these pastilles. It is the method of Professor E. Rupp, which was first described in *Archiv de Pharmazie*, Vol. 244, page 536. In this elegant method the corrosive sublimate by means of KOH and KI is changed to mercuric-potassium iodide, which with solution of formaldehyde, is reduced to metallic mercury. Diluted acetic acid is then added, as this will prevent any decomposition of tenth normal iodine volumetric solution by the excess of formaldehyde. The iodine solution dissolves the metallic mercury, forming mercuric iodide. The excess of iodine is titrated with tenth normal sodium thiosulphate volumetric solution, from which the amount of mercuric chloride is calculated. Unlike other assays, the red aniline dye Eosine does not interfere with the determination of mercuric chloride in the Rupp assay.

The object of the addition of sodium chloride to the tablet is two-fold: it increases its solubility and it furthermore neutralizes the acid reaction of mercuric chloride. A double salt is formed, namely $\text{HgCl}_2 \cdot 2\text{NaCl}$, which is neutral. For the formation of this double salt 100 parts of HgCl_2 requires 43 parts of NaCl, consequently 57 parts of NaCl are in excess.

The colorless bichloride tablets have been responsible for the great many accidents which have occurred of late in different parts of the United States. Methylene blue has been recommended and has been used for coloring these tablets and solutions. As pointed out by Thomas Wilson, in the *Pharmaceutical Journal*, 1913, page 99, abstracted in *The Practical Druggist*, May, 1913, page 39, methylene blue forms a precipitate with bichloride solutions which are stronger than 1 in 1000. Red has always been considered as a danger signal, and for that reason a red color is to be preferred to a blue or green color in a bichloride tablet, besides being more permanent. The German Pharmacopoeia does not specify the amount of the red aniline dye, but manufacturers are in the habit of using 1 gram of Eosine to 1 kilogram of the mixture.

The German Pharmacopoeia specifies a cylindrical shape, namely, twice as long as thick. This requirement was evidently for the purpose of preventing confusion between the deadly bichloride tablets and any other harmless round tablets.

The foresight of the German authorities can well be seen in the requirement that each tablet must be wrapped individually with black paper, which in white letters bears the word "Poison."

The amount of mercuric chloride must also be stated on each black wrapper with white letters, giving the number of grams contained in each tablet. This is a new requirement in the fifth edition of the German Pharmacopoeia.

The tablets must be kept in the poison closet under lock and key. They must be protected from the light, as this might in time bleach the color somewhat, and they must also be protected from moisture, as the sodium chloride in the tablets is apt to absorb same.

Bichloride tablets must be dispensed in well-closed amber bottles, which must bear a poison label. It is furthermore customary that the German apothecary caution the patient regarding the poisonous nature of these tablets and advise him to keep them under lock and key.

Last, but not least, the sale of these tablets in Germany is restricted to prescriptions only. They cannot be sold to every Tom, Dick and Harry, and this precaution undoubtedly accounts for the fact that no poisonings, accidental or suicidal, with bichloride tablets occur in Germany.

The author has procured tablets of different manufactures in different parts of Germany which are herewith submitted. The danger to the public is unquestionably largely overcome in the German bichloride tablet. No one can possibly swallow such a tablet accidentally during the day or night. The German bichloride pastilles are practically "fool proof."*

It is one of the first duties of the pharmacist to be careful in order to prevent error or to minimize the danger in dispensing poisons. Be careful! This should be the watchword of every pharmacist.

This paper, together with the specimens, may serve as an illustration of how well the German government and the German pharmacist take care of the health and safety of the public. No heterogeneous laws in different parts of the German Empire, but a pharmacopoeial standard and requirement to which every manufacturer and every pharmacist *has to live up to* and *does live up to*.

Let the German bichloride tablet serve as an illustration for our great country and its Pharmacopoeia, so that the latter may deserve the title "Peer of all Pharmacopoeias."

*The writer, however, cannot help but express his great surprise that such a standard work as *Hager's Handbook der Pharmazeutischen Praxis*, nor its supplement, has any comments to make on *Pastilli Hydrargyri Bichlorati*. Merely the formula is stated but no comparisons are made and no comments are given. Truly not a credit to this master work of pharmacy.