

BICHLORIDE OF MERCURY TABLETS AND BICHLORIDE TABLET LEGISLATION.*

GEORGE M. BERINGER, PH. M.

In presenting a paper on such a hackneyed subject as Bichloride of Mercury Tablets and Bichloride Tablet Legislation, I am well aware that I may be trying your patience on a subject that you may perhaps consider as threadbare. My association with and study of this subject, however, convinces me that this is not a dead subject, but that it contains several problems directly associated with the duties of the druggist and which pharmacists themselves, in a very large measure, must decide.

The extensive use of corrosive sublimate in this form has justified the decision of the Committee of Revision of the U. S. P. to introduce an official formula, and by this means to endeavor to provide additional safeguards to life in their use. The articles that have appeared in the medical, pharmaceutical and lay press, as well as the discussion in the committee, demonstrate that this is a live subject and associated with it are several questions still to be settled.

In the official recognition of the tablet of mercuric chloride, the U. S. P. is only following the example of most of the pharmacopœias that have been revised in recent years. A study of the foreign formulas and a comparison of these, and likewise of the commonly used American formulas, is interesting.

In American practice, either Wilson's formula, containing a mixture of mercuric chloride and ammonium chloride, or Bernay's formula, containing mercuric chloride and citric acid, have been almost exclusively used. In Europe the formula proposed by Angerer, for *Pastilla Hydrargyri Bichlorati*, has been the type followed. His formula is the following:

PASTILLI HYDRARGYRI BICHLORATI.

Mercury bichloride.	
Sodium chloride.....aa	0.5 Kg.
Eosin	1.0 Gm.

Mix the salts and color the mixture with the eosin dissolved in water. Allow the mixture to dry in the air and compress into portions, weighing one or two grammes each.

The German Pharmacopœia IV (1900), and, again in the fifth edition (1910), adopts the title "*Pastilli Hydrargyri Bichlorati*" and directs that, from a mixture of equal parts of mercuric chloride and sodium chloride colored with a red coal tar dye, are to be made cylinders twice as long as thick and weighing 1 or 2 gm. each. Sublimate pastilles must be dispensed in sealed bottles labelled "Poison," and each pastille must be wrapped in black paper on which is printed, in white, the word "Poison" and the content of mercuric chloride stated in grammes.

The Swedish Pharmacopœia (1901) under the title of "*Pastilli Chloreti Hydrargyrici*" directed that "Sublimate pastilles" should be hard cylinders or prisms, weighing either 1 or 2 gm. each, and composed of equal parts of mercuric

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chloride and sodium chloride and colored red by an aniline dye. It, likewise, introduced the requirement, that each tablet must be wrapped in black paper, on which was printed in white the word "Poison."

The Austrian Pharmacopœia (1906), under the title "Pastilli Hydrargyri Bichlorati Corrosivi," directed that equal parts of mercuric chloride and sodium chloride should be triturated to a thorough mixture and colored with a solution of eosin and compressed in pastilles weighing 1 gm. to 2 gm. The pastilles are directed to be dispensed in glass bottles, under a poison-label, and the pastilles are to be singly wrapped in black paper with the word "Poison" imprinted in white.

The Swiss Pharmacopœia, (1907), adopted as a title "Hydrargyrum Bichloratum Compressum," and, as a synonym, "Pastilli Sublimati." The formula is mercuric chloride 666 gm., sodium chloride 333 gm., eriocyanin, A, 1 gm., mixed and compressed into tablets weighing 37.5 cg., 75 cg. and 1.5 gm., and containing, respectively each 25 cg., 50 cg. and 1 gm. of corrosive sublimate. It directs that each tablet must be wrapped in black paper on which is printed, in white, the weight of the sublimate contained, the word "Poison" and a death's-head design.

The British Pharmaceutical Codex, in the first edition of 1907, and likewise in the 1911 edition, gave formulas for a series of these tablets. Under the name of "Solvellæ Hydrargyri Perchloridi,—Soluble Mercuric Chloride Tablets," and, as synonymous, "Antiseptic Perchloride, or Corrosive Sublimate Tablets,"—it directed a mixture of equal parts of mercuric chloride and sodium chloride colored with methyl violet, to be compressed into tablets containing 8.75 grains of the mercuric chloride, so that one dissolved in the imperial pint (20 fl. oz.) of water, will make a one-tenth percent (1 in 1000) solution of mercuric chloride. Under the title "Solvellæ Hydrargyri Perchloridi Fortes," or "Strong Soluble Mercuric Chloride Tablets," a tablet of the same percentage of essential ingredients, but double the weight, was directed, so that one tablet dissolved in twenty fluid ounces of water makes one-fifth percent (1 in 500) of mercuric chloride. Other formulas are given for a "mild" and for a "small" soluble mercuric chloride tablets, yielding, when dissolved as directed, solutions containing 1 in 4000 and 1 in 4500, the latter being especially recommended as suitable for ophthalmic purposes.

The French Pharmacopœia (1908), presented a new style of formula for use of mercuric chloride in antiseptic solution. Its formula for "*Papier au Chlorure Mercurique*" or "*Charta hydrargyri bichlorati*" directs that 5 gm. each of mercuric chloride and sodium chloride be dissolved in a sufficient quantity of distilled water to obtain a volume of 20 cc. Filter paper, purified by treating with water containing one part of hydrochloric acid to the thousand, washing with pure water and drying, is then saturated with the mercuric chloride solution, so that each rectangular surface, 5 cm. by 10 cm., shall imbibe 1 cc. of the solution and represent 25 cg. of mercuric chloride. The superscription "Corrosive Sublimate, twenty-five centigrammes," is directed to be printed with indigo-carmine, thus producing, when immersed in the proper volume of water, a blue solution. The paper is to be protected from light and moisture, and the container is to be labeled in indelible red letters "Poison."

These specifications of the *Pharmacopée Française*, official in that country since July 17, 1908, yields a product essentially the same as the corrosive sublimate leaflets now being made by an American manufacturer, who claims originality and the right to a patent thereon as a new and novel invention.

The Italian Pharmacopœia (1909), gives the title "*Pastiglie di Cloruro Mercurico*," with the Latin synonym, "Pastilli Bichlorureti Hydrargyri." The formula is mercuric chloride and sodium chloride equal parts, colored with an aqueous solution of eosin, and compressed into circular pastilles of 1 or 2 gm. in weight.

It is to be noted that most of the foreign pharmacopœias, have, simply, followed in their titles the nomenclature proposed by Angerer, and designate these tablets as "Pastilles." In the same pharmacopœias, the title "pastilli" is frequently applied to mild remedial agents dispensed in the form of confections or lozenges. It is certainly an unfortunate designation and a dangerous classification that would include such a toxic form along with worm-lozenges, cough-troches, peppermint-drops, etc. It is still more to be regretted that it has been proposed to adopt this same title in the U. S. P. IX. The use of the word "pastille" in this connection is not in accordance with the English usage of this word. As defined in the dictionaries, the word "pastille" refers to several forms of substances of an entirely different character and dissimilar use.

The Century Dictionary defines "pastille" or "pastil"—

"1—a small roll of aromatic paste, composed of gum benzoin, sandal wood, spices, charcoal powder, etc., designed to be burned as a fumigator.

"2—a kind a sugared confection, usually of a strong flavor, of a round flat shape, like peppermint drops.

"3—in art: (a) a thin round cake of watercolor; (b) the method of painting with watercolors prepared as pastils or a drawing produced by them.

"4—In pyrotechny: a paper case filled with a burning composition intended to cause rotation of a wheel."

Neither of these definitions would comprise a mercuric chloride tablet of the shape described, or its intended use. In medicine and pharmacy, this title had already been pre-empted and used to a considerable extent for medicated confections, and its adoption, for such a toxic official preparation, is an exceedingly dangerous experiment. It was probably for this reason that the *Pharmacopœia Helvetica* adopted as its title, "*Hydrargyrum Bichloratum Compressum*," and the British Pharmaceutical Codex, "*Solvellæ*." The "*Solvellæ*" of the Codex, are compressed tablets or discs intended to be dissolved in water for external or local use. The attempt at classification here made, is a step in the right direction. The title coined, however, does not include the toxic character of the product, and, moreover, is subject to the criticism that it has the appearance of an attempt to imitate the trade-marked name of a certain brand of tablets extensively used in England.

The necessity is for a distinct title that will clearly differentiate between the medicinal tablets used so extensively for internal administration, and poisonous tablets intended for external use. The safeguarding of life is the first and principal consideration, and this warrants the coining of a new title, that shall distinguish the latter as a separate and distinct class. For this purpose, I propose *Toxibellæ* as a distinctive class title, and as the official title for these

tablets, *Toxitabellæ Hydrargyri Chloridi Corrosivi*, and as the English, Poison Tablets of Corrosive Mercuric Chloride.

The foreign formulas follow the formula of Angerer, in directing equal parts of mercuric chloride and sodium chloride. The American manufacturers generally claim on their labels to adhere to the Wilson formula. Tablets containing the proportion of ammonium chloride directed in this latter formula, are prone to change on keeping. They deliquesce in humid atmospheres and the solubility also lessens with age. For these reasons, some of the manufacturers have already substituted sodium chloride for part of the ammonium chloride. One manufacturer advises that he has found preferable a mixture of corrosive sublimate 7.3 parts, ammonium chloride 2.7 parts, sodium chloride 5 parts. The entire replacement of the ammonium chloride by sodium chloride will doubtless yield a more stable and soluble tablet, and this change should be adopted in the pharmacopœial formula.

The coloring of bichloride of mercury antiseptic tablets, was originally proposed, not only to make them distinct in color from other tablets of the same shape and size, but the primal idea was to obtain a solution that would have a distinct color and not be mistaken and administered for harmless medications or for water. Such accidents had occurred and to prevent their recurrence, Angerer proposed, as an additional safeguard, that solutions of corrosive sublimate should be colored. It has been difficult to select a red dye that would possess sufficient tinctorial-strength, so that only a minute quantity of the coloring agent would be required, and at the same time would be permanent and not altered by the action of the chemicals nor fade on keeping. This problem has confronted the manufacturers and has been the subject of considerable experimentation on the part of the writer.

Eosin, in the quantity proposed, yields a tablet that is distinctly pink, but when in solution (1 in 1000) it does not show a distinct color. This practical difficulty with the red dyes, their variable shades, and, moreover, the fact that confections are frequently of this color and liquid medicines are likewise, commonly, some shade of red, has led to the use of other colors. The British Pharmaceutical Codex directs methyl violet, which, in this combination, gives a blue-purple solution. The Swiss Pharmacopœia orders eriocyanin A, the sodium salt of a sulphonated dye of the triphenyl-methane-carbinol type, that colors silk and wool a bright blue, and is only slightly affected by 10 percent. hydrochloric acid. The French Codex directs Indigo-Carmine for this purpose.

A number of the manufacturers are already giving preference to the blue tablets. One of these manufacturers writes: "Green and red-colored tablets are not at all satisfactory. I believe that you will agree with me that a somber blue would prove the most desirable. Confections are made in red, green, yellow, white and every conceivable color, but the blue is not attractive and, therefore, would in all probability prove the safest."

On the question of coloring for mercuric chloride, Dr. A. G. Rosengarten, whose firm prepares large quantities of mixed salts, already colored for the manufacturers, writes me:

"The only satisfactory color that we have found is blue dye, called indigo-

carmine. We have not yet found a satisfactory red or green dye, but I can highly recommend indigo carmine for consistent results, and a definite weight of that dye added to a definite weight of corrosive sublimate mixture, will produce definite results. I cannot say the same about the other dyes, and I think it will be most desirable to confine the dyes for corrosive sublimate mixture to the one color, blue, and the one dye, indigo-carmine."

My own experiments confirm these statements as to the availability of indigo-carmine for this purpose. 2.5 mg. per tablet is sufficient to color 500 Cc. of water a distinct blue. If a more intense color be desired, this can be increased up to 5 mg. and the quantity to be specified in the formula for 100 tablets should not exceed .5 gm. In my experiments with red dyes, iod-eosin and alizarin carmine (sodium alizarin sulphonate) appear to have given the best results, with the Wilson type, but the color of the solutions is not as bright a red as might be desired. With the Bernay formula, containing citric acid, methylorange has shown the best results.

The official tablet should be adjusted to the basis of one tablet to 500 Cc. of water, yielding a 1 in 1000 solution, instead of one tablet to the pint, as has been the custom. This will necessitate only a slight increase in the weight.

The shape to be adopted for the official "Bichloride Tablets" is one of the questions that is being considered. When these tablets were introduced, the manufacturers, quite naturally, used the moulds already in use, and so the unfortunate mistake was made of manufacturing these poisonous tablets of the round or disc shape; the same shape and size as were used for innocuous medicinal tablets and confections. Fatal accidents, attributable in part to the shape, have demonstrated that it is imperative that this dangerous practice should be discontinued. Toxic tablets of the bichloride of mercury antiseptic type, should be made in a unique shape, one that has not been used for any other purpose, and the use of such a shape or form should be restricted, by legal enactments, to toxic tablets intended for external use.

In recent years, the ingenuity of the American manufacturer has been exercised to obtain a distinctive shape that should characterize and distinguish his brand of "antiseptic tablets." As a result, we now have such shapes as the triangle, diamond, square, cube, keystone, and clover leaf, exploited as proprietary forms of antiseptic tablets. Every one of these shapes has been commonly used in confections and their official recognition and continuance for bichloride antiseptic medication would be a repetition of the original fatal error as to the shape of such tablets. The manufacturers of these shapes are each clamoring for the recognition of his particular shape.

The influence of these commercial interests has been exerted to prevent legislative action that would designate an appropriate shape, or judicial consideration that would permit judgment to crystallize in favor of an official shape, that would insure the greatest amount of protection to life. After all, the question of "safety first" is the paramount question.

Of all the proposals for a shape for bichloride of mercury tablets, the coffin shape suggested by Mr. F. M. Apple in his paper before the Pennsylvania Pharmaceutical Association seems to be best. This has already been adopted by at least four manufacturers, and its general adoption has only been prevented by

the commercial interests back of other designs. Commercial instincts and financial advantage, and not the broad humanitarian principle of what is best to protect life, have been the causes actuating the opposition to legislation and to the official recognition of the best suggestion yet offered.

The German Pharmacopœia has been quoted, as an authority to be followed in fixing the U. S. P. standard. I believe that we should appropriate from the foreign pharmacopœias all that our experience and judgment prove to be correct and in accordance with American practice. In this instance, I cannot approve of following the *dictum* of the German Pharmacopœia. I have a sample of the official German Corrosive Sublimate tablets that have been in my possession since last March. These are not uniform in color and fading has commenced to take place. The shape is in conformity with that of the Ph. Gr., twice as long as broad, and the manufacturer to show this, and possibly to permit of economy, in using only half a tablet at a time, has made them with a ridge across the centre. This makes them resemble forms of the pink, linked phenolphthalein, and other proprietary, laxative wafers, that are so extensively used in this country. It would be difficult to conceive of a more dangerous experiment, than to officially recognize such a shape for bichloride tablets. It would be on a par with the adoption of the Italian Pharmacopœial standard of the round tablet, which we are now ready to condemn. There is no uniformity in the European pharmacopœias regarding these tablets, and so the argument, for the adoption of an international standard, falls flat. The solution of these tablets, when made of a strength of 1 to 1000, as commonly used, is of so delicate a pink tint as to be barely perceptible.

So far as I know, no American manufacturer has yet placed on the market, a bichloride of mercury tablet copied after that of the German Pharmacopœia. As this formula has been published for more than fourteen years, this is noteworthy, and may be construed as an evidence of the good judgment of our manufacturers. To now insist, that the U. S. Pharmacopœia should adopt and make legal, a shape that has not met favor in American practice, is a unique proposition that lacks the popular approval that is essential to its effectiveness.

The importance of throwing every safeguard possible around the sale and handling of such poisonous substances, is now thoroughly recognized. The newspapers have given wide publicity to the deaths, either suicidal or accidental, occurring from bichloride tablets. The evils resulting from the overzealous newspaper, which gives its readers all the details of the method by which some poor unfortunate has gone on the long voyage, have been discussed and decried, yet nevertheless it continues its course with little or no abatement.

A number of State legislatures, in session during the past year, have had under consideration, laws that would restrict the handling of such poison tablets, and which would define their shape, color and label, and further prohibit the use of the prescribed shape for any other purpose. There are, at least, three bills, on the same subject, now pending in Congress. It is certain that we may expect legislation before long on this entire matter, and it is eminently proper that the drug trade should take an active interest in solving a question of public safety that is so closely associated with our business. Unfortunately, the atti-

tude assumed by some of the druggists is that of thoughtless indifference. The argument advanced by others is that such legislation is only a passing sentimental fad and that it can have no influence on the protection of life. This is so fallacious, that it can not long continue to prevent legislation.

It was never expected that any legislation would prevent a person of morbid mind from committing suicide. This is not the purpose of the proposed legislative enactments, but it is contended that, in prescribing a distinctive shape for these poison tablets, they could under no circumstances be mistaken, either in the day or night, for harmless medications. If a distinctive shape had been supplied the Macon, Ga., banker and the Brooklyn business-man, whose deaths, beyond question, were accidental poisonings, at least these lives could have been spared. The necessity for a distinctive shape for Bichloride of Mercury Tablets is well shown by the compilation appearing in Public Health Report No. 46, by Martin I. Wilbert of the United States Public Health Service. In this compilation, Mr. Wilbert shows that, at that time, in the current price-lists of five leading pharmaceutical manufacturers, there were sixteen different formulas and varying sizes of poison bichloride tablets, five different shapes, five different colors, and only three, out of the sixteen, were then made of any other shape than the ordinary round tablet used for internal medication, such as headache and cold tablets. Could any stronger evidence of the necessity for restrictive legislation and a distinctive shape for these poison tablets, be presented, than this compilation in a government bulletin, which shows the present dangerous and unsatisfactory method of marketing these tablets?

The influence of certain manufacturers on proposed legislation, is shown in the act passed by the last session of the Maryland Legislature. Instead of specifying in the act a distinctive shape or color, the value of the legislation enacted is largely nullified by the amended form in which the bill was passed. This law provides that "tablets containing more than 1/10 grain of Mercury Bichloride, must be of either triangular, diamond, square, oblong or other irregular shape, and their color must be either blue, purple, or green, with the word "Poison" imprinted or embossed on each tablet." Further, these tablets can only be sold, dispensed or given away, in bottles, upon one side of which the word "Poison" has been blown, and with a label with the word "Poison" placed on the face of the bottle.

The restrictions regarding the package and labeling, are such as are commonly employed by all of the manufacturers, but the very needed protection *to the consumer*, has been lost sight of, by the overpowering commercial-spirit that prevented the selection of a distinctive shape for the tablets. Any one of a number of shapes, is equivalent to no shape, and the very indefiniteness of the act as passed destroys its value as a measure for the safety of the public.