

the graduate represents the volume of gas liberated from the spirit. Calculate as directed in the U. S. P.

One source of error with this apparatus is that it is impossible to displace all the air from the 8-ounce bottle, about one cubic centimeter remaining. This, reacting with the gas generated causes a contraction in volume. But as the air is only one-fifth oxygen the error cannot be greater than one-fifth of a cubic centimeter. This is not greater than the error in the official nitrometer which is due to the fact that the saturated salt solution in the reservoir side of the nitrometer has a specific gravity of about 1.200 while twenty-five cubic centimeters of that in the calibrated side of the nitrometer has a specific gravity of about 1.000.

For practical purposes it is sufficient to ascertain that one cubic centimeter of the spirit evolves eleven cubic centimeters of gas. This is equivalent to about four per cent, or the mean of the pharmacopœial requirement and it would only be under abnormal conditions that barometric pressure would cause this to be above or below the official limit of toleration.

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## A PHARMACEUTICAL STUDY OF MAGMÆ MAGNESIÆ—1900–1930.

BY A. J. LEHMAN, M.S.

*Historical.*—**Magma Magnesiæ** (Milk of Magnesia) made its official appearance in the N. F. III (1906). Previous to this little information can be found in the literature available, relative to this preparation. Aqueous suspensions of magnesium oxide were known and used at an earlier date, an example of which is the *Magnesia usta in aqua* in the 1871 Hungarian Pharmacopœia. In 1874, Wilder (1) offered a Calcined Magnesia Mixture consisting of 1 part of light calcined magnesia to 12 parts of water. The same year another writer (2) suggested the following formula for "milk of magnesia:"

Calcined magnesia	8 parts
Water	40 parts
Sugar	50 parts
Orange flower water	20 parts

The same article includes a formula for "Lac Magnesiæ" from the 1831 Schleswig-Holstein Pharmacopœia, as follows:

Calcined magnesia	2 parts
Rub uniform with distilled water	10 parts
Heat to boiling with constant stirring	
Remove from fire and add,	
Powdered white sugar	12 parts
Orange flower water	4 parts

The Report on the Progress of Pharmacy (3) in 1881 includes the following statement under the heading of Milk of Magnesia: "Triturate 2 parts of calcined magnesia with well boiled or distilled water. Preserve in well-stoppered vials." Dietrich (4)

(1885) five years later offered a "new formula" for "Milk of Magnesia" consisting of 10 parts of calcined magnesia to 100 parts of distilled water. In 1891, Fleury (5) suggested preparing "Magnesium hydrate" by mixing solutions of magnesium sulphate and of sodium hydroxide. The precipitate was washed and then dried at a moderate temperature. A British product (6) (1896) called Liquid Magnesia was prepared by mixing solutions of sulphate of magnesia and of sodium carbonate, washing and collecting the precipitate, mixing this with water and saturating the mixture with CO<sub>2</sub>. The product was stored in tightly stoppered bottles to "prevent loss of CO<sub>2</sub>." In 1900 S. B. (7) called attention to the use of the name Milk of Magnesia to a suspension of magnesium hydroxide in water. The trade patent to this name had expired in 1890. Three years later Scoville (8) (1903) offered the following formula for a Milk of Magnesia:

Magnesium sulphate	250 Gm.
Sodium hydroxide	81 Gm.
Water, a sufficient quantity to make	1000 cc.

The two chemicals were dissolved in separate portions of water, then mixed; the precipitate washed, collected and suspended in distilled water. One teaspoonful of the finished product was to contain about 3 Gm. of magnesium hydroxide. F. S. K. (9) in 1904 mentions a formula given in the "Standard Formulary" which differs from the above in ratio of ingredients and in the use of "Solution of Potassa." He also suggests that a quick method for preparing Milk of Magnesia consists of mixing light calcined magnesia 510 grains, glycerin 3½ ounces and water 11½ ounces. The formula offered by Scoville (8) (1903) was adopted by the N. F. III (1906). Whereas the formula and directions were quite simple, the products varied much when prepared by different pharmacists. Furthermore the manipulations as directed brought forth a number of criticisms and suggestions. As a result of the investigations the formula for Milk of Magnesia has met with several changes during the last two revisions of the official standards containing this product. In this paper an attempt has been made to present a comparative analysis of the official formulas together with a summary of such comments on this product as found in the literature available. It may be of interest to know that 110 articles were abstracted exclusive of the comments found in the *U. S. P. Revision Circulars*. This it is assumed does not represent all of the articles published.

#### 1. TITLES AND SYNONYMS.

Milk of Magnesia was introduced into the N. F. III (1900) under the Latin title of **Magma Magnesiae**. The 1910 and 1920 revisions of the U. S. P. retained it under the same title. The English title for both texts was *Magnesia Magma*. The synonym *Milk of Magnesia* appears in both standards. The 1910 revision of the Pharmacopœia introduced the official abbreviation **Magma Mag.**, which is retained by the 1920 revision.

Foreign Pharmacopœias have not introduced this preparation to any extent. The following is a list of titles obtained from the Pharmacopœias and other official standards:

"British Pharmaceutical Codex" (1923): *Mistura Magnesii Hydroxidi*, *Cremor Magnesia*, *Cream of Magnesia*, *Emulsi Magnesia*, *Emulsion of Magnesia*, *Lac Magnesiae*, *Mixture of Magnesium Hydroxide*.

"French Pharmacopœia" (1908): Magnesium (Hydroxide De), Hydrate de Magnesia, Magnesii Hydratii, Magnesium Hydroxydatum.

In commenting on the titles for the magma Raubenheimer (10) (1907) suggests the following title: **Magnesii Hydroxidum Precipitum Plutiforme**, while Diehl (11) (1909) suggests that the title be changed to **Mistura Magnesii Hydroxidi**, and Needham (12) (1910) favors **Cremor Magnesiæ**. Hommell (13) (1920) favors dropping the synonym Milk of Magnesia, "milky magnesia" would be more desirable. The former synonym he suggests is unscientific inasmuch as the product is not like milk outside of its color.

## 2. DEFINITION AND PURITY RUBRIC.

The purity rubric for milk of magnesia in the 1900 N. F. called for "about 3 grains of magnesium hydroxide to a teaspoonful." Taking an ounce of the magma as weighing 480 grains, 3 grains would represent about 5% of  $Mg(OH)_2$ . The 1910 revision of the U. S. P. increased the strength. It specifies that the magma must contain not less than 6.5% and not more than 7.5%  $Mg(OH)_2$ . This equivalent to about 3.9 to 4.5 grains in a teaspoonful. The 1920 revision changed the purity rubric to read "not less than 7 per cent of  $Mg(OH)_2$ ;" representing about 4.2 grains per teaspoonful. (A fluidounce of a commercial milk of magnesia weighed 500 grs.) In commenting on the *Purity Rubric* Terry (14) (1919) suggests changing the requirement to 5.5 per cent, since the amount of sodium hydroxide prescribed is insufficient to produce 6.5 per cent of  $Mg(OH)_2$ . On the other hand Hilton (15) (1920) favors increasing the requirement to 7.5 per cent of  $Mg(OH)_2$ , while Lyons (16) (1920) favors 8 to 8.5 per cent of  $Mg(OH)_2$  as such a product would be less liable to separate. In commenting on the report by Army (17) (1920) that the purity rubric should be changed to "not less than 7 per cent  $Mg(OH)_2$ ," Scoville (18) (1920) calls attention to the possible lack of uniformity because no maximum requirement is given.

## 3. PRESERVATION.

The National Formulary makes no statement relative to the preservation of Milk of Magnesia. The 1910 and 1920 revisions of the U. S. P. direct that the magma must be kept in wide-mouth bottles tightly stoppered with corks which have been dipped in melted paraffin.

This protective measure of coating the cork with paraffin is undoubtedly to prevent the action of  $Mg(OH)_2$  on the cork, which would discolor the preparation. Hensel (19) (1915) asserts that in order to preserve the magma properly rubber stoppers should be used.

## 4. MAGNESIUM SULPHATE OR MAGNESIUM CARBONATE AS AN INGREDIENT.

The 1900 revision of the N. F. prescribed 250 Gm. of magnesium sulphate for the preparation of 1000 cc. of magma. The 1910 revision of the U. S. P. replaced the magnesium sulphate with magnesium carbonate, prescribing 125 Gm. for 1000 cc. of magma. The 1920 revision of the U. S. P. again directed the use of magnesium sulphate prescribing 300 Gm. for 1000 cc. of magma.

The purity rubric for magnesium sulphate and for magnesium carbonate is as follows:

1900—"Not less than 99.7 per cent of  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  or 48.84 per cent anhydrous  $\text{MgSO}_4$ ."

1910—"A mixture of hydrated magnesium carbonate and magnesium hydroxide corresponding to not less than 39.3 per cent of  $\text{MgO}$ ."

1920—"Not less than 48.60 per cent and not more than 53.45 per cent of  $\text{MgSO}_4$ , corresponding to not less than 99.5 per cent of crystallized salt ( $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ )."

Based on the purity rubric 250 Gm. of magnesium sulphate represent 121.73 Gm. of absolute  $\text{MgSO}_4$ ; 125 Gm. of magnesium carbonate represent 49 Gm. of  $\text{MgO}$ ; and 300 Gm. of magnesium sulphate represent 145.80 to 160.45 Gm. of  $\text{MgSO}_4$ . Furthermore:

I	$\text{MgSO}_4$ equivalent to	$\text{MgO}$ equivalent to	$\text{MgCO}_3$
	120.38 equivalent to	40.32 equivalent to	84.32 or,
	1.00 equivalent to	0.344 equivalent to	0.700 then,
	121.73 equivalent to	40.77 equivalent to	85.25 (N. F. 1900)
	145.80 equivalent to	50.15 equivalent to	102.06 (U. S. P. 1920)
	160.45 equivalent to	55.16 equivalent to	112.32 (U. S. P. 1920)
II	$\text{MgO}$ equivalent to	$\text{MgSO}_4$ equivalent to	$\text{MgCO}_3$
	40.32 equivalent to	120.34 equivalent to	84.32 or,
	1.00 equivalent to	2.985 equivalent to	2.091 then,
	49.00 equivalent to	146.25 equivalent to	102.46 (U. S. P. 1910)

#### SUMMARY TABLE.

Year.	Magnesium sulphate.	Magnesium carbonate.	$\text{MgSO}_4$ .	$\text{MgCO}_3$ .	$\text{MgO}$ .
1900	250		121.73	85.23	40.77
1910		125	146.25	102.46	49.00
1920	300		145.80	102.06	50.15
			160.45	112.32	55.16

A difference of opinion occurred as to the correct amount of magnesium sulphate to be used. Raubenheimer (20) (1907) advocates using only 240 Gm. of magnesium, decreasing the excess, thereby leaving less to wash out. Posey (21) (1909) suggests a reduction to 224 Gm. while Diehl (22) the same year recommends 220 Gm. Hilton (23) (1911) offers a formula in which 350 Gm. of magnesium sulphate is prescribed. (The amount of alkali is increased.) Mueller (27) (1917) suggests using 270 Gm. of magnesium sulphate dried, representing about 552 Gm. of the crystalline salt. (The amount of sodium hydroxide is also increased.) A formula offered (24) (1920) prescribes 500 Gm. of magnesium sulphate for 1000 cc. of magma. Beringer (25) (1920) in commenting on this calls attention to the proposed purity rubric, *viz.* 6.5 to 7.5 per cent  $\text{Mg}(\text{OH})_2$ . Using 500 Gm. of magnesium sulphate the yield would be "11.83 Gm.  $\text{Mg}(\text{OH})_2$  in each 100 cc." Little has been said on the use of magnesium carbonate. McNeery (26) (1916) suggested the use of 9212.46 grains of magnesium carbonate representing about 149.4 Gm. for 1000 cc. of magma. Mueller (27) (1917) and Corfield (28) (1923) both suggested the use of magnesium oxide in place of the carbonate.

#### SUMMARY TABLE.

Formula.	Magnesium carbonate.	Magnesium sulphate.	Purity rubric.	Absolute.
N. F. 1900		250 Gm.	48.59%	121.475 Gm. $\text{MgSO}_4$
U. S. P. 1910	125		39.20	49.0 Gm. $\text{MgO}$
U. S. P. 1920		300 Gm.	48.60	145.8 Gm. $\text{MgSO}_4$
			to	to
			53.45	160.45 Gm. $\text{MgSO}_4$

Raubenheimer	240 Gm.	48.59	116.616 Gm. MgSO <sub>4</sub>
Boehm	250 Gm.	48.59	121.475 Gm. MgSO <sub>4</sub>
Bruder	250 Gm.	48.59	121.475 Gm. MgSO <sub>4</sub>
Posey	224 Gm.	48.59	108.841 Gm. MgSO <sub>4</sub>
Diehl	220 Gm.	48.59	106.898 Gm. MgSO <sub>4</sub>
Hilton	350 Gm.	48.59	170.065 Gm. MgSO <sub>4</sub>
Beringer	250 Gm.	48.59	121.475 Gm. MgSO <sub>4</sub>
Mueller	270 (anhyd.)	99.50 (?)	268.65 Gm. MgSO <sub>4</sub>

(To be continued)

## SYRUP OF FERROUS IODIDE AND THE OFFICIAL HYDRIODIC PREPARATIONS.\*

BY H. V. ARNY, BENJAMIN VENER AND LESLIE C. JAYNE.

### INTRODUCTION.

The question of the stability of syrup of ferrous iodide and of syrup of hydriodic acid and of the diluted acid itself has been the subject of many papers. Of these at this time we will mention only papers by Haussmann (1), Alpers (2), Beringer (3), Dunning (4) and Base (5) on syrup of ferrous iodide and those by Raubenheimer (6), Sieker (7) and Lane (8) as far as syrup of hydriodic acid is concerned.

The recent pharmacopœial revision work of one of the present authors brought the subject once more to his attention from the standpoint of stability of these preparations and of their assay and the experiments reported below represents a study of the question over a period of four years:

### Part I.

#### SYRUP OF FERROUS IODIDE.

(Work performed with Benjamin Vener, Ph.G., B.S.)

Four samples of this syrup were prepared:

A. Exactly as directed in U. S. P. IX. The fresh sample assayed 5.436 per cent of ferrous iodide.

B. As directed by U. S. P. IX with omission, however, of the hypophosphorous acid. The fresh sample assayed 5.436 per cent of ferrous iodide.

C. U. S. P. proportions of iron and iodine, hypophosphorous acid omitted, sugar 80 Gm., glycerin 70 Gm. to 250 Gm. of finished syrup. The fresh sample was not quite up to the U. S. P. requirements, assaying 4.325 per cent of ferrous iodide.

D. Iron wire, 3.2 Gm.; iodine, 10.4 Gm.; diluted hypophosphorous acid, 5 cc.; sugar, 100 Gm.; glycerin, 55 Gm.; water to make 250 Gm. The fresh sample assayed 4.921 per cent of ferrous iodide.

Samples A and B were prepared on September 25, 1924. Half of each batch was poured into small, completely filled bottles which were opened only as they were assayed. The other half of each batch was kept in its original container and was assayed regularly; hence was exposed to the action of the air. Sample C was prepared November 23, 1924, and successive samples were drawn from the original

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