(3) Beringer, *Ibid.*, 3 (1914), 970.

(4) Dunning, "Proc. Md. Pharm. Assoc.," through PROC. A. PH. A., 52 (1904), 573.

(5) Base, *Ibid.*, 52 (1904), 573.

(6) Raubenheimer, PROC. A. PH. A., 51 (1903), 384.

(7) Sieker, *Pharm. Rev.*, 20 (1902), 518.

(8) Lane, *Am. J. Pharm.*, 79 (1907), 366.

(9) Snyder, *et al.*, "Proc. A. D. M. A.," 9 (1920), 251.

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A PHARMACEUTICAL STUDY OF MAGMÆ MAGNESIÆ—1900–1930.

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(Continued from p. 265, March Issue).

5. SODIUM HYDROXIDE AS AN INGREDIENT.

Sodium hydroxide is prescribed by all three standards containing Magma Magnesia. The 1900 N. F. prescribed 81 Gm., the U. S. P. of 1910, 80 Gm. and the U. S. P. revision of 1920 increased the amount to 100 Gm., each for 1000 cc. of product. The purity rubric for the last three revisions reads "not less than 90 per cent of NaOH." Based upon this 81 Gm., 80 Gm. and 100 Gm. of sodium hydroxide represent 72.9 Gm., 72 Gm. and 90 Gm. of NaOH. Other alkalies were suggested in place of sodium hydroxide. An unsigned article (29) (1896) includes a formula for a "Fluid magnesia" in which sodium carbonate is prescribed. A second formula (30) (1904) prescribes "solution of potash—enough."

Raubenheimer (31) (1907) in commenting on this ingredient prefers NaOH to KOH in preparing milk of magnesia because of the greater solubility of the formed sodium sulphate which makes it easier to wash out. Terry and Davy (32) (1920) are also in favor of sodium hydroxide because of the cost. Ammonia should not be used they claim as magnesium hydroxide is soluble in ammonia. Grosh (33) (1913) contrary to this statement says that using stronger ammonia water, gives a more rapid precipitation and also eliminates filtering.

In respect to the quantity of sodium hydroxide used Bruden (34) (1909) suggests increasing the sodium hydroxide by one-half while Diehl (35) (1909) suggests a reduction to 72 Gm. Cloughy (36) (1913) increases the quantity to 81 Gm., Hilton (37) (1911) to 119 Gm. and Beringer (38) (1913) to 100 Gm. McNeery (39) (1916) for one gallon of magma uses 6259.08 grains or about 405 Gm., representing about 101 Gm. per 1000 cc. Mueller (40) (1917) offers an increase to 120 Gm., Boehm (41) (1908) to 125 Gm.

The following table summarizes the quantities of sodium hydroxide directed to be used by the official as well as by non-official formulas together with the respective absolute equivalents.

Formula.	Sodium hydroxide.	Purity rubric.	Absolute.
N. F. 1900	81	90%	72.9 Gm. NaOH
U. S. P. 1910	80	90	72.0 Gm. NaOH
U. S. P. 1920	100	90	90 Gm. NaOH

Formula.	Sodium hydroxide.	Purity rubric.	Absolute.
Raubenheimer	81	90	72.9 Gm. NaOH
Boehm	125	90	112.5 Gm. NaOH
Posey	81	90	72.9 Gm. NaOH
Bruden	121.5	90	112.95 Gm. NaOH
Diehl	72	90	64.8 Gm. NaOH
Hilton	119	90	107.1 Gm. NaOH
Beringer	100	90	90 Gm. NaOH
Mueller	120	90	108 Gm. NaOH

6. RATIO OF INGREDIENTS.

The following equation may be used to represent the reaction taking place when the Magma is prepared according to the National Formulary process.

$$(1) \quad MgSO_4 + 2NaOH + Mg(OH)_2 + Na_2SO_4$$
$$120.39 \quad 80.02$$
$$1 \quad \cdot 0.664$$
$$121.475 \quad 79.9$$
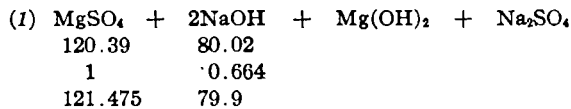
Inasmuch as only 72.9 Gm. of NaOH are prescribed, the theoretical deficiency is 7.0 Gm.

$$(2) \quad 2NaOH + MgSO_4 = Mg(OH)_2 + Na_2SO_4$$
$$80.02 \quad 120.39$$
$$1 \quad 1.504$$
$$72.9 \quad 109.641$$
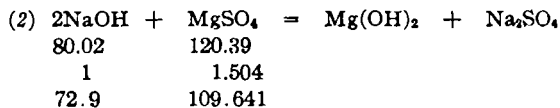
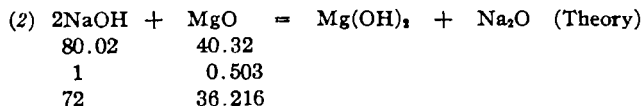Inasmuch as 121.475 Gm. of $MgSO_4$ are prescribed, the excess present is 10.83 Gm.

The equation representing the reaction taking place when the Magma is prepared according to the U. S. P. 1900 method may be represented by the following:
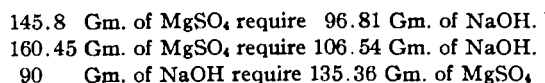
$$(1) \quad MgO + 2NaOH = Mg(OH)_2 + Na_2O \quad (Theory)$$
$$40.32 \quad 80.02$$
$$1 \quad 1.94$$
$$49 \quad 97.216$$
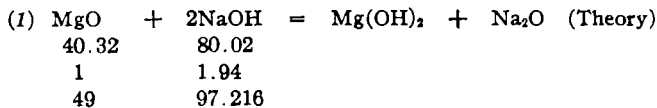
Inasmuch as only 72 Gm. of NaOH are prescribed the theoretical defficiency is 25.216 Gm.

$$(2) \quad 2NaOH + MgO = Mg(OH)_2 + Na_2O \quad (Theory)$$
$$80.02 \quad 40.32$$
$$1 \quad 0.503$$
$$72 \quad 36.216$$

Inasmuch as the equivalent of 49 Gm. of MgO is prescribed the equivalent MgO in excess is 12.784 Gm.

The U. S. P. revision of 1920 reverted to the use of magnesium sulphate. Based upon the equations given above:

145.8 Gm. of $MgSO_4$ require 96.81 Gm. of NaOH.
160.45 Gm. of $MgSO_4$ require 106.54 Gm. of NaOH.
90 Gm. of NaOH require 135.36 Gm. of $MgSO_4$.

Hence there is prescribed an excess of 10.44 Gm. to 25.09 Gm. of $MgSO_4$ or a deficiency of 6.81 Gm. to 16.54 Gm. of NaOH occurs.

From the above the following becomes apparent, *viz.:* (*a*) That according to the N. F. process the amount of Magnesium Hydroxide in the finished product is that represented by 109.641 Gm. of MgSO₄. (*b*) That according to the U. S. P. 1910 process the amount of Magnesium Hydroxide in the finished product, that resulted from the interaction between the salt and the alkali is that represented by 72 Gm. of NaOH. (*c*) That according to the U. S. P. 1920 process the amount of Magnesium Hydroxide present in the finished product is that represented by 135.36 Gm. of MgSO₄.

Based upon this the following becomes apparent:

(*a*) $MgSO_4$ = $Mg(OH)_2$
120.39   58.04
1   0.484
109.6   53.065 Gm. of $Mg(OH)_2$ in 1000 cc. of product.
(*b*) $2NaOH$ = $Mg(OH)_2$
80.02   58.34
1   0.729
72   52.788 Gm. of $Mg(OH)_2$ in 1000 cc. of product.
(*c*) $MgSO_4$ = $Mg(OH)_2$
120.39   58.34
1   0.484
105.36   65.514 Gm. of $Mg(OH)_2$ in 1000 cc. of product.

SUMMARY TABLE.

Formula.	NaOH.	MgSO₄.	MgSO₄ required.	Excess.	Mg(OH)₂ in 1000 cc.
N. F. IV	72.9	121.475	109.641	10.80	53.06 Gm.
U. S. P. 1910	90.0	14.58	135.36	10.44	65.51 Gm.
		160.45		25.09	
Raubenheimer	72.9	166.16	109.641	56.519	53.06 Gm.
Boehm	112.5	121.475	168.75	. . . . .	53.06 (NaOH in excess)
Bruder	112.95	121.475	169.50	. . . . .	53.06 (NaOH in excess)
Diehl	64.8	106.898	97.20	9.698	47.05 Gm.
Hilton	107.10	170.065	160.63	9.435	70.74 Gm.
Beringer	90.0	121.475	135.36	. . . . .	53.06 (NaOH in excess)
Mueller	108.0	268.65	162.4	106.25	51.42 Gm.
Posey	72.9	108.84	109.641	. . . . .	52.67 Gm.

7. WATER.

The N. F. 1900 does not specify that distilled water be used in the preparation of the magma. It does, however, state in a note that "the water used in preparing this must be free from organic matter or the magma will become discolored."

The U. S. P. 1910 prescribes that distilled water be used throughout the entire process. It also includes a note which states, "the distilled water in this preparation may be replaced by water which has been heated to boiling with powdered Magnesium Carbonate, 5 Gm., in 1000 mils and then filtered." The revision of 1920 prescribes distilled water.

Distilled water is somewhat expensive for the average pharmacist to use and various suggestions have been made to overcome this obstacle. Raubenheimer (42) (1907) says water used in preparing the magma must be free from organic matter. He suggests using Scoville's (43) (1903) method of purifying it, that of adding 2 grains of alum to each gallon of water to precipitate the organic matter. Cliffe (44)

(1910) experimented with filtered river water but found the magma became dis-
colored. Beringer (45) (1913) states that if distilled water cannot be obtained,
water which has been boiled with magnesium carbonate 5 Gm. to 1000 cc. will
prove satisfactory. Needham (46) (1910) mentions using hot water previously
boiled to free from organic matter.

8. METHOD OF PREPARATION.

A. Solution or Suspension of the Magnesium Salt.—The N. F. 1900 formula
calls for 4000 cc. (or 128 ounces) of water to dissolve the magnesium sulphate.
The U. S. P revision of 1910 directs that the magnesium carbonate be mixed with
sufficient distilled water to make a smooth mixture, about 500 cc. being sufficient
and the revision of 1920 prescribes distilled water to make 650 cc. The concen-
tration of this solution has brought about numerous comments. Bruder (47) (1909)
reduces the volume to 500 cc. in order to obtain a heavier precipitate when the two
solutions are mixed; Hilton (48) (1911) follows this closely by dissolving the salt in
400 cc. of distilled water. Beringer (49) (1913) prescribes 1000 cc., while
Mueller (50) (1917) directs using 700 cc. of water.

B. Solution of Sodium Hydroxide.—The N. F., 1900, prescribes 4000 cc. (or
128 ounces) of water for the solution of the sodium hydroxide. The U. S. P.
revision of 1910 called for 400 mils of distilled water while the revision of 1920
prescribes sufficient distilled water to make 1000 cc. In commenting on the N. F.
formula Bruder (51) (1909) reduces the volume to 500 cc. Hilton (52) (1911) pre-
scribes 700 cc.; Beringer (53) (1913) 1000 cc. and Mueller (54) (1910) only 250 cc.
Other concentrations are offered for both solutions of magnesium sulphate and
sodium hydroxide, but all practically come within the two extremes reported here.

C. Order of Mixing the Solutions.—According to the N. F. 1900 the two solu-
tions are filtered separately and then the Sodium Hydroxide solution poured
"slowly and in a thin stream into the Magnesium Sulphate solution with constant
stirring." According to the U. S. P. 1910 the sodium hydroxide solution is added
to the Magnesium Carbonate mixture, with constant stirring and frequent agita-
tion during 15 minutes, and the revision of 1920 again directs the addition "slowly"
of the sodium hydroxide to the magnesium sulphate solution. Caldwell (55) (1906)
favors a reversal of the order, claiming a better magma, whereas Dunn (56) (1911)
emphasizes the pouring of the alkali solution into the magnesium sulphate solution
"in a fine stream and with constant stirring." Beringer (57) (1913) supports Dunn
claiming an advantage of an excess of alkali during the precipitation. Others
supporting this order of mixing are Hensel (58) (1914) and Mills (59) (1914).

D. Hot or Cold Solutions.—No mention of the use of heat is made in the
formulas of 1900 and 1910. The U. S. P. revision of 1920 directed that the magne-
sium sulphate solution be boiling and that the boiling be continued for thirty min-
utes after the addition of the sodium hydroxide solution. Caldwell (60) (1906)
directed the use of hot solutions. Beringer (61) (1913) also favors hot solutions
and Cloughy (62) (1913) prescribes a temperature of 70° C. Possehl (63) (1914)
directs heating the solutions after mixing, slowly stirring and boiling for 15 minutes.
Hensel (64) (1914), Mills (65) (1914) and Hilton (66) (1911) all favor hot solutions.

E. Washing the Magma.—The N. F. 1900 directs that the magma should be
washed by decantation until the washings are free from saline taste. The U. S. P.

1910 states: "Wash the resulting magma by decantation using two thousand mils of water each time until the red color produced in 50 mils of the washings by 3 drops of phenolphthalein T. S. is discharged by one drop of diluted sulphuric acid," while the U. S. P. 1920 simply directs the use of sufficient hot distilled water, washing repeatedly until the washings show no sulphates with barium chloride T. S. Apparently most of the comments deal with the technique of washing rather than the volumes of wash water used. Raubenheimer (67) (1907) suggests removing the water by syphoning; Boehm (68) (1908) suspends the magma in an inverted percolater and washes by percolation. This procedure is approved of by Diehl (69) (1909) and Beringer (70) (1910). Hilton (71) (1911) dilutes the magma to 3000 cc. and allows it to settle to the 1000 mark, syphons off the supernatant liquid, again adding 2500 cc. of water, repeating this twice followed by the addition of 4000 cc. for the final washing. Hensel (72) (1914) washes with five times as much distilled water, as the volume of finished product, doing this about five times. McNeery (73) (1916) directs washing the precipitate by either decantation or siphoning until the washings are neutral to litmus. Hensel (74) (1915) finds four washings sufficient and Terry (75) (1919) washes the hot magma by boiling with twice as much water as product desired, and repeating twice.

F. Collecting the Magma.—According to the N. F. 1900 the magma is collected on a muslin strainer, allowed to drain without pressing, then transferred to suitable vessels and sufficient water added to make 1000 cc. The U. S. P. 1910 directs that the magma be allowed to subside till it measures 1000 cc. and the supernatant liquid decanted, while the revision of 1920 prescribes concentration "by evaporation" to required volume.

Raubenheimer (76) (1907) states that the precipitate should not be drained because of danger of CO_2 absorption. Sennewald (77) (1907) reports difficulty in obtaining a precipitate that could be collected on a strainer. Furthermore that the "settling" takes place so slowly. Boehm (78) (1908) suggests placing the magma in a percolator, then fastening a layer of cheese cloth over the mouth, inverting, washing and collecting the magma in this manner. Hilton (79) (1911) directs that the washed magma be allowed to subside to the required volume. Beringer (80) (1913) calls for a muslin strainer for collecting the precipitate while Hensel (81) (1915) favors a filter paper and the removal of the precipitate with a silver spoon. Sayre (82) (1917) reports that three weeks would be required to wash and collect the precipitate according to the U. S. P. directions. That the final subsidation required nearly a week alone; the use of a centrifuge facilitates the collection of the magma.

The U. S. P. 1920 directs "concentrate the mixture by evaporation until it contains not less than 7 per cent of magnesium hydroxide" may not be a solution of the difficulty. No temperature is mentioned and as one may assume from the differences of opinion as to the use of heat in making the magma, the application of varying temperatures for evaporation may influence the nature of the final product.

(To be concluded)