A PHARMACEUTICAL STUDY OF MAGMÆ MAGNESIÆ—1900-1930.

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9. QUALITATIVE TESTS.

A. Description and Physical Properties.—The N. F. 1900 makes no statement relative to the appearance of the finished product. The U. S. P. 1910 states the magma is "a thick white liquid containing Magnesium Hydroxide in suspension in water," and the revision of 1920 states, "a viscous, opaque, white mixture, from which more or less water usually separates on standing; free from mustiness."

The appearance of the product is an important criterion. Pharmacists apparently have difficulty in obtaining a magma having the desired color and consistency. Boehm (83) (1908) in commenting on this states that the N. F. product is too thick to pour, also that some manufacturers add magnesium oxide to insure a white color. Posey (84) (1909) reports difficulty in obtaining a white product, as does Hensel (85) (1914). Beringer (86) (1913) suggests a possible discoloration due to impurities in the wash water.

B. Tests for Identity.—1. *Alkalinity.*—The N. F. 1900 gives no qualitative tests for Magma Magnesia. The U. S. P. 1910 and 1920 state that the Magma is alkaline to litmus and phenolphthalein. This alkalinity according to an article (87) (1911), prevents the use of gelatin as a suspending agent. The latter being more susceptible to mold growth if in an alkaline medium.

2. Test for Magnesium.—Both revisions of the U. S. P. apply the same test for "magnesium" with slightly varying technique. A precipitate of magnesium ammonium phosphate results. The reactions may be expressed as follows:

$$Mg(OH)_2 + 2HCl = MgCl_2 + 2H_2O$$
$$MgCl_2 + NH_4OH + Na_2HPO_4 = MgNH_4PO_4 + 2NaCl + H_2O$$

3. Tests for Purity.—a. Test for CO_2.—Both the revisions of the U. S. P. state that there must be no evolution of gas on the addition of 2 mils of diluted hydrochloric acid, and the resulting solution should not be more than slightly turbid. The evolution, if any, would be caused by the presence of magnesium or calcium carbonate. This seems to be one of the lesser difficulties in preparing the magma, for many preparations made in the laboratory were tested, all giving negative results. The reaction occuring may be expressed as follows:

$$MgCO_3 + 2HCl = MgCl_2 + H_2O + CO_2$$
$$CaCO_3 + 2HCl = CaCl_2 + H_2O + CO_2$$

b. Test for the Limit of Soluble Compounds.—According to the U. S. P. of 1910, 10 mils of the magma are diluted with 100 mils of distilled water and the precipitate allowed to settle. The water dissolves any soluble impurities and the residue obtained from evaporating 50 mils to dryness on a water-bath must not weigh more than 0.005 Gm. The revision of 1920 dilutes 20 cc. of the magma with 200 cc. of distilled water after which the procedure is the same as above. The 5 mg. of residue may be accounted for by a slight suspension of the $Mg(OH)_2$ or due to its slight solubility.

c. Test for Limit of Soluble Alkali.—According to the U. S. P. 1910 the residue obtained from the previous test when redissolved in water and methyl orange T. S. added, not more than 5 drops of $N/1$ H_2SO_4 shall be required to neutralize the alkalinity. The revision of 1920 required that not more than 0.4 cc. of $N/10$ H_2SO_4 shall be required to neutralize 50 cc. of the supernatant liquid obtained from the above test, using methyl orange T. S. as indicator. Any excess of this is looked upon as being sodium hydroxide. Terry (88) (1919) found that magma carefully prepared by the U. S. P. process had an alkalinity corresponding to 11.2 mils of $N/10$ H_2SO_4. He says the U. S. P. limits this to "4 mils." He suggests the foreign alkalinity be determined by titrating the supernatant liquid of a diluted magma rather than by evaporation. His method is to dilute 25 mils of magma with 175 mils of water and after shaking and settling titrate the supernatant liquid. He also suggests that a test for arsenic and for the determination of heavy metals be included, and that a portion of the magma be ignited to determine the presence of carbonizable material.

10. ASSAY.

The N. F. 1900 gives no assay for Magma Magnesia. The U. S. P. 1910 offers the following:

"Transfer about 5 Gm. of Magma Magnesia to a tared flask, stopper and weigh accurately, add 25 mils of normal sulphuric acid T. S., and after solution is complete titrate the excess of acid with normal potassium hydroxide T. S. using methyl orange T. S. as indicator. It shows an amount of magnesium hydroxide corresponding to not less than 6.5% nor more than 7.5% of the weight of Magnesia Magma taken.

"Each mil of normal sulphuric T. S. used corresponds to 0.02917 Gm. of $Mg(OH)_2$. Each Gm. of Magnesia Magma corresponds to not less than 2.23 mils nor more than 2.57 mils of normal potassium hydroxide T. S."

Sulphuric acid reacts with magnesium hydroxide to form magnesium sulphate and water as follows:

$$H_2SO_4 + Mg(OH)_2 = MgSO_4 + 2H_2O$$

Potassium hydroxide reacts with sulphuric acid to form potassium sulphate and water as follows:

$$2KOH + H_2SO_4 = K_2SO_4 + 2H_2O$$

Hence $Mg(OH)_2$ equivalent to H_2SO_4 equivalent to 2KOH

58.34 ——2000 cc. $N/1$ V. S.——2000 cc. $N/1$ V. S.

0.02917——1 cc. $N/1$ V. S.

then

$$\frac{2.23 \times 0.02917}{1} \times 100 = 6.5\%$$

$$\frac{2.57 \times 0.02917}{1} \times 100 = 7.5\%$$

The revision of 1920 offers the same method of assay, using sodium hydroxide V. S. in place of potassium hydroxide V. S.

As early as 1911, Craig (89) recognized the value of an official assay process. Hilton (90) (1911) outlines a method consisting of adding to 10 cc. of magma 30 cc.

of $N/1$ H_2SO_4 V. S. and 2 drops of phenolphthalein T. S., heating the solution and determining the excess of acid with $N/1$ KOH V. S., each cc. of $N/1$ H_2SO_4 V. S. representing 0.2897 Gm. $Mg(OH)_2$. LaWall (91) (1914) suggests that the simplest assay would be by evaporation, but this would give variable results due to the variable stages of dehydration which the product assumes as it dries. He then offers a method comparable to the present U. S. P. assay, using however, only 3 Gm. of magma, 25 cc. $N/2$ HCl V. S., $N/1$ KOH V. S. and phenolphthalein as the indicator. Terry (92) (1919) in commenting on the U. S. P. assay favors the use of phenolphthalein T. S. in place of the prescribed methyl orange T. S.

Some of the results of assay are as follows: Ewe (93) (1913) reports samples 20% above strength as designated on label. LaWall (94) (1914) reports a range of 2.22% to 9.57% for 12 samples. Snapp (95) (1918) rejected 9 out of 13 samples. Terry (96) (1918) states that an analysis of proprietary brands showed a range of 5.21% to 9.79%. In 1920 Terry (97) reports 33 out of 62 samples meeting the U. S. P. test. The range was from 4.41 to 8.37. Miller (98) (1921) found one out of three samples below standard.

11. SUSPENDING AGENTS.

Only one formula is given in the available literature for preparing a magma containing a suspending agent. Gelatin is used in this instance. This formula given by Hilton (99) (1911) is as follows:

Magnesium sulphate	350 Gm.
Sodium hydroxide	119 Gm.
Gelatin	0.15 Gm.
Distilled water q.s.	1000 cc.

Dissolve the sulphate in 400 cc. water and filter. Dissolve the gelatin in 50 cc. hot water and add to the sulphate solution.

Dissolve the NaOH in 400 cc. water, cool and add 300 cc. water. When both have cooled add the NaOH to the sulphate in such a manner as to deliver the alkali in rapid drops. After all is added dilute to 3000 cc., allow to settle to 1000 mark, decant, add 2500 cc. water, decant. After two more such operations 4000 cc. are added, allowed to settle to 1000 mark, decanted, assayed and diluted if necessary.

An objection to the use of gelatin as a suspending agent has already been mentioned (see alkalinity).

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ERGOT ALKALOIDS.

Ergot Alkaloids and Their Actions. A. STOLL, Meeting Deut. Pharmakol. Gesellsch. Hamburg (9/12/28); *Klin. Wochschr.*, 7 (1928), 2223, No. 46, through *Squibb Abstract Bulletin.*

In a discussion following an illustrated lecture by Barger on the development of the ergot alkaloids and their actions, Stoll stated that amorphous ergotoxin and crystalline ergotamine appear identical in pharmacological examination, but the question of chemical identity has not as yet been solved. In spite of great similarities (same absorption spectra, etc.), there are also detectable differences, such as a difference of C_2H_4 in the formula. The conversion of ergotoxin and its derivatives (ergotinine) into ergotamine and vice versa has not been effected. Further chemical and physical-chemical data on these substances are to be obtained.—E. G.