

Some men have attempted to judge the viability of these cultures by examinations for motility under the microscope, forgetful of the fact that the Bulgarian Bacillus is non-motile. Others have attempted to stain a smear of the culture and have also met with failure because there is not sufficient albuminous material in the media to properly fix the bacteria to the slide. If a few drops of the culture be mixed with a large drop of egg white or Mayer's Albumin Fixative and the two well mixed and smeared, if this smear be dried, fixed by heat, stained by Gram's method and examined under the high power of the microscope, a fairly good estimate may be made of the number of viable bacilli. All dead bacilli stain a Gram negative while those which are still viable are Gram positive. This interpretation will have to be modified in case the involution forms appear, as they generally stain as negative, even when living and capable of growth.

It is needless to say that the majority of the druggists to-day are making strong efforts to furnish their trade with potent biological products and are providing facilities for the storage of perishable articles at a reasonably low temperature; and it is the loyal coöperation of this class of pharmacists that makes possible the marketing of dependable cultures of Bulgarian Bacillus.

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ANALYSES OF MILK OF MAGNESIA.*

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Due to the wide variation of the declared content of magnesium hydroxide in the various standard brands of Milk of Magnesia, and the silence of other manufacturers as to the content, the writer became interested to know how many of these standard brands conformed to the U. S. P. IX or to the former standard, the N. F. III. It was with this object in view that these analyses were made.

Table A shows the percentage of Magnesium Hydroxide in the leading seven brands and five control samples—one prepared according to the U. S. P. IX, one according to the N. F. III, one according to Beringer's process¹ modified by

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¹ Geo. M. Beringer, *Proc. N. J. Ph. A.*, 1913, pp. 46-48.

the writer, and two prepared from magnesium oxide. It will be noted that these seven standard brands vary from 5.22 percent to 9.79 percent $\text{Mg}(\text{OH})_2 w/w$ or from 23.9 to 44.9 grains per fluidounce. The U. S. P. demands from 6.5 percent to 7.5 percent $\text{Mg}(\text{OH})_2 w/w$ or from 29.7 to 34.4 grains per fluidounce, while the former standard, the N. F. III, is 24 grains to the fluidounce or 5.23 percent w/w .

It is a deplorable fact that manufacturers will market a product that is as easily assayed as milk of magnesia with absolute disregard for official standard.

TABLE A.

No.	Source.	$\text{Mg}(\text{OH})_2 w/w$.	Carbonates.	Foreign alkalinity. ¹	Sp. gr. C 25 C. ²	Remarks.
1	Proprietary.....	5.71%	Ft. trace	6.4 mils N/10 V. S.	...	Not U. S. P. or N. F. ³
2	Pharm. house.....	8.53%	Ft. trace	6.4 mils N/10 V. S.	...	Not U. S. P. or N. F.
3	Pharm. house.....	7.37%	Ft. trace	8.0 mils N/10 V. S.	...	U. S. P. except foreign alkalinity ⁴
4	Pharm. house.....	8.42%	Ft. trace	11.2 mils N/10 V. S.	...	Not U. S. P. or N. F. ⁵
5	Pharm. house.....	5.22%	Ft. trace	7.2 mils N/10 V. S.	...	Not U. S. P. Exactly N. F. ⁶
6	Drug syndicate...	6.73%	Ft. trace	9.6 mils N/10 V. S.	...	U. S. P. except foreign alkalinity
7	Pharm. house.....	9.79%	Ft. trace	6.4 mils N/10 V. S.	...	Not U. S. P. or N. F.
8	N. F. III.....	3.22%	Ft. trace	3.2 mils N/10 V. S. ⁷	1.010	Not N. F. ⁸
9	U. S. P. IX.....	3.52%	Ft. trace	6.4 mils N/10 V. S. ⁹	1.011	Not U. S. P.
10	Prep. MgO.....	6.24%	Present	6.4 mils N/10 V. S.	...	Not U. S. P. or N. F.
11	Comm. MgO.....	4.83%	Trace	4.8 mils N/10 V. S.	...	Not U. S. P. or N. F.
12	Mod. Beringer...	4.42%	None	7.3 mils N/10 V. S.	...	Slightly below N. F.

¹ Amount contained in 100 mils of magma. ⁶ Claimed 24 grains to fluidounce, found 23.96.

² Approximate.

⁷ N. F. contains excess of sulphate.

³ Claimed 24 grains to fluidounce, found 26.2. ⁸ Should be 24 grains, assayed 14.78.

⁴ Claimed 32 grains to fluidounce, found 33.8. ⁹ Washings corresponded to U. S. P. acid test.

⁵ Claimed 40 grains to fluidounce, found 38.6.

There are only two of the seven that conform to the U. S. P. IX, and two that conform to the N. F. III. Although several of them declare a different standard on their labels, it should be in bold type and not in the reading matter. The writer does not approve of the U. S. P. IX standard for the preparation, yet the manufacturers should consider the standard for the sake of uniformity and justice to the public, if for nothing else. Milk of magnesia is widely used to delay the coagulation of cows' milk in the infant's stomach and a slight variation of alkalinity here will retard or accelerate the coagulation far more than is proportional to the concentration of the alkali. So it will be seen that this variation is really of more importance than is at first apparent.

In assaying milk of magnesia, phenolphthalein is the proper indicator, rather than methyl-orange as is directed by the U. S. P. IX. If the methyl-orange is added to the magma before acidification, the methyl-orange acts like certain organic coloring materials in the presence of certain metallic hydroxides and forms a magnesium lake. This substance has no property of an indicator and upon acidification the indicator property is not restored. If the methyl-orange is added after acidification of the magma, the influx of the alkaline volumetric solution causes momentarily a precipitate of magnesium hydroxide which partially destroys the methyl-orange, and under these conditions, the end point is anything but definite.

None of the samples contained excessive carbonates as shown by the U. S. P. IX test except No. 10, which was made from a magnesium oxide which is marketed especially for preparing milk of magnesia.

In testing for foreign alkalinity, the writer did not use the official process, namely—that of evaporation of the supernatant liquid from a dilute magma to constant weight and titration of the residue. The writer's method is to mix 25 mls of magma with 175 mls of distilled water and titrate the supernatant liquid, using phenolphthalein as indicator. This is quite a saving of time and at no expense of accuracy. The figures for foreign alkalinity in Table A are the number of mls of $\frac{N}{10}$ acid required to neutralize the foreign alkalinity of 100 mls of the magma. The U. S. P. limits this to 4 mls, whereas the above preparations in every case except one contained more than this (even up as high as 11.2 mls). Sample No. 9 was prepared strictly according to the U. S. P. IX and the washings corresponded to the dilute sulphuric acid drop test, yet the product exhibits a foreign alkalinity of 6.4 mls per 100 mls of magma.

In the U. S. P. IX process, the magnesium hydroxide is produced by the interaction of sodium hydroxide and magnesium carbonate, sodium carbonate being the only by-product of the reaction, it is far easier to titrate sodium carbonate than to evaporate the liquid to constant weight and then titrate. It requires only a few seconds to ignite a part of the magma in a porcelain crucible to determine if any starch, sugar, gum or mucilaginous substances are present. Their presence would be indicated by carbonization. I presume this is the object of evaporating to constant weight in the official foreign alkalinity test.

The specific gravity of this U. S. P. IX magma is 1.011 and the N. F. III magma is 1.010 at 25° C.

It is agreeable to note that two of the marketed samples claimed 24 grains to the fluidounce and these assayed 26.2 and 23.96 grains, respectively; one claimed 32 grains and assayed 33.8 grains; one claimed 40 grains and assayed 38.6 grains; one claimed 46 grains and assayed 44.9 grains. It is significant to note that samples prepared according to the U. S. P. IX and the N. F. III fell way below the desired strength. The U. S. P. IX sample contained only 3.52 percent $Mg(OH)_2$ while it should be between 6.5 percent and 7.5 percent. The N. F. III sample contained only 3.22 percent while it should be 5.23 percent. Sample No. 10, that prepared by a special magnesium oxide for this purpose, assayed 6.24 percent, while it should be about 8.5 percent, that is, according to the manufacturer's statement. Sample No. 11, prepared from a commercial magnesium oxide, assayed 4.83 instead of being 7 percent as desired. Sample No. 12, that prepared by Beringer's process but washed by the writer's procedure, assayed 4.42 percent instead of being 5.23 percent as desired. Charles H. LaWall gives results of assays of milk of magnesia with practically identical results. The variation in the content of magnesium hydroxide was over 300 percent.²

In the preparation of sample No. 12, the magma is precipitated by pouring the hot magnesium sulphate solution into the hot sodium hydroxide solution, maintaining a degree of alkalinity throughout the precipitation that ensures complete precipitation of the magnesium, which does not occur in the N. F. III

² Chas. H. La Wall, JOURNAL A. PH. A., 1914, pp. 1002-1003.

process where the procedure is reverse, in the cold.³ Beringer's process contains an excess of about 10 percent alkali, which is proper. The writer modified Beringer's process only in washing the magma, endeavoring to formulate an extemporaneous process. As the precipitation is conducted at boiling temperature, the magma filters rapidly, so that as soon as precipitation is complete, the whole may be poured at once on a filter paper and allowed to drain; the magma is then transferred back to the vessel and distilled water added equal to double the volume of desired magma; the mixture is then boiled and refiltered, this being repeated again twice; then the washings will conform to the U. S. P. IX dilute sulphuric acid drop test. It is true that considerable magnesium hydroxide is lost due to the several transferrings necessary, but what was desired here, was to see how rapidly a milk of magnesia could be prepared, which was accomplished in three hours. Washing in this manner, although probably not feasible on a large scale, would be of considerable advantage to the pharmacist because of the rapidity of production and the use of a minimum amount of distilled water, which is one of the reasons that few retailers make their own milk of magnesia. It is quite possible that milk of magnesia could be washed by dialysis on a commercial scale, and if so, it would have several advantages over the decantation method.

The quantitative relations of the sodium hydroxide and magnesium sulphate in the N. F. III formula are in error, as it requires 81.5 grammes of absolute sodium hydroxide to precipitate 250.0 grammes of magnesium sulphate. The N. F. process calls for only 81.0 grammes of U. S. P. sodium hydroxide, which is only 90 percent absolute sodium hydroxide, so that there is a deficiency of alkalinity amounting to a little over 10 percent making it impossible to prepare a magma from the N. F. formula containing over 4.7 percent $Mg(OH)_2$. There is always considerable magma lost mechanically in siphoning off the supernatant liquid and in transferring the magma from the strainer. But, peculiarly, if all the 250.0 grammes of magnesium sulphate were precipitated, it would produce theoretically a magma containing 5.9 percent magnesium hydroxide less than mechanically lost.

The preparation of milk of magnesia by hydrating the oxide has proven a failure in the hands of the writer and also several manufacturing pharmacists. It is almost impossible by this method to secure complete hydration, some of the oxide remaining unhydrated and suspended throughout the mixture. A macroscopic examination of the mixture will show its semi-granular nature. Milk of magnesia prepared by this process seems to cake on standing.

In the U. S. P. IX process, there is an alkaline carbonate medium for the precipitation, yet the magma seems to be composed of both oxide and hydroxide which does not give the proper viscosity to the product and, furthermore, it requires eight to ten washings to remove the alkalinity. If the hydration of the magnesium carbonate is intended to be performed by the sodium hydroxide only, and not by absorption of water in the reaction, which is probably the case, then the U. S. P. formula would require for the 125.0 grammes of magnesium carbonate, based on the following reaction, 82.37 grammes of absolute sodium hydroxide to ensure complete hydration of the carbonate:

³ Sam. T. Hensel, JOURNAL A. PH. A., 1914, pp. 1118-1120.

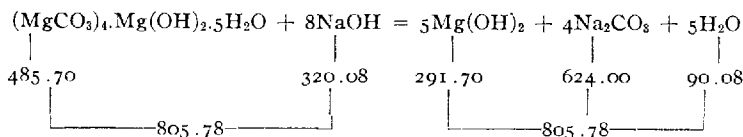


TABLE B.

No.	Sulphates.	Chlorides.	Heavy metals, ¹	Arsenic trioxide. ²	Talcum.	Ignition.	Hot and cold permanganate.	
							Acid.	Alkaline.
1	Small amount...	None	Minute trace	Faint trace	None	No carbonization	No reaction	No reaction
2	None.....	None	Present	Faint trace	None	No carbonization	No reaction	No reaction
3	Trace.....	None	Minute trace	Faint trace	None	No carbonization	No reaction	No reaction
4	Trace.....	None	Present	Faint trace	Present	No carbonization	No reaction	No reaction
5	Faint trace....	None	Present	None	None	No carbonization	No reaction	No reaction
6	None.....	None	Trace	None	None	No carbonization	No reaction	No reaction
7	None.....	None	Minute trace	Faint trace	None	No carbonization	No reaction	No reaction
8	Present ³	None	None	None	None	No carbonization	No reaction	No reaction
9	None.....	None	Minute trace	None	None	No carbonization	No reaction	No reaction
10	None.....	None	Minute trace	Faint trace	None	No carbonization	No reaction	No reaction
11	None.....	None	Minute trace	Faint trace	None	No carbonization	No reaction	No reaction
12	Present ⁴	None	Trace	None	None	No carbonization	No reaction	No reaction

¹ U. S. P. IX test.

² U. S. P. IX test.

³ BaCl₂ test; precipitates slightly.

⁴ Does not precipitate. BaSO₄ remains suspended.

The U. S. P. formula calls for 80 grammes of U. S. P. sodium hydroxide, the equivalent of 72 grammes of absolute sodium hydroxide, a deficiency of 10.37 grammes of absolute sodium hydroxide. The U. S. P. IX formula should have at least 91.52 grammes of U. S. P. sodium hydroxide, the equivalent of 82.37 grammes of absolute sodium hydroxide, to ensure complete hydration, and to have an excess of sodium hydroxide in the formula 100.0 grammes is about the proper amount to use. Then the formula will theoretically produce a magma containing 7.507 percent of magnesium hydroxide. "The official formula, known as McNeary's formula, has proven somewhat unsatisfactory in our hands, etc."⁴

The writer believes the production of milk of magnesia by the interaction of magnesium sulphate and sodium hydroxide is far superior to the U. S. P. IX process. The degree of gelatinization of the hydroxide may be controlled by the dilution of the solutions that are to be mixed and the temperature of the mixing. The magnesium hydroxide should be as gelatinous as possible and still maintain fluidity; in this condition we have pharmaceutical elegance combined with maximum therapeutic activity. Due to the minute state of subdivision of the magma, it exhibits maximum activity and does not separate so readily on standing.

Table B gives results of tests for sulphates, chlorides, heavy metals, arsenic, talcum, and the application of ignition and acid and alkaline permanganate tests. The samples were tested for sulphates to determine which were prepared by the sulphate method and to determine the extent to which the magmas were washed. The samples were tested for chlorides to determine if distilled water was used in washing the magma. Three of the magmas marketed by pharmaceutical houses contained more heavy metals than allowable by the U. S. P. IX tests. None of the preparations contained as much as the allowable limit of arsenic, 1-100,000, based on 1-100,000 of the magnesium hydroxide content of the magmas. Talcum was present in one marketed product and how it could be present, and why, is

⁴ Nat. Stand. Disp., 1916, p. 983.

not understandable. None of the products were carbonized on ignition, thus probably showing the absence of sugar, starch, gum, etc. None of the preparations reacted with acid or alkaline permanganate, thus showing the absence of glycerin, sugar, etc. Sample No. 1 gave no ether soluble extractive matter, thus showing the absence of flavoring oils.

Table C shows results of a microscopic examination of the magmas which readily shows the difference of the physical state of the magnesium hydroxide produced by the different processes. Several of the samples contained small acicular crystals resembling sodium sulphate but what the crystals were was not determined.

TABLE C.

MICROSCOPIC EXAMINATION OF MILK OF MAGNESIA.

No.	Result.
1	Particles in minute state. No crystals.
2	Magma fairly finely divided. No crystals.
3	Magma finely divided, same as No. 1, occasional acicular crystals.
4	Resembles gelatinized starch. Acicular crystals present.
5	Exceedingly fine magma. No crystals.
6	Magma very fine, occasional small crystals.
7	Resembles small gelatinized starch grains. No crystals.
8	Particles in minute state. No crystals.
9	Resembles gelatinized starch grains. No crystals.
10	Resembles gelatinized, large, starch grains. No crystals.
11	No examination made.
12	No examination made.

From the above data, information is gleaned that may be useful to the Revision Committee of the U. S. P. X, as follows:

1. That milk of magnesia be prepared by interaction of magnesium sulphate and sodium hydroxide and that the sodium hydroxide be in excess of the theoretical amount to at least 10 percent.
2. That tests be conducted to determine the feasibility of washing the magma by the hot process as above suggested, or by dialysis.
3. That the purity rubric read, magnesia magma yields not less than 5.0 percent nor more than 5.5 percent of $Mg(OH)_2$ (58.34).
4. That the limit of permissible foreign alkalinity be raised to the equivalent of 8.0 mils of $\frac{N}{10}$ V. S. to 100 mils of magma.
5. That the foreign alkalinity be determined by titration of the supernatant liquid from a diluted magma rather than by evaporation.
6. That a portion of the magma be ignited in a porcelain crucible to determine the presence or absence of carbonizable organic matter.
7. That a test be included to limit the presence of heavy metals.
8. That a test be included to limit the presence of arsenic.
9. That the process be made so as to form a magma containing as high as 6 percent $Mg(OH)_2$ if possible and that it be then assayed and diluted to meet the purity rubric.⁵
10. That the assay process be identical with that of the U. S. P. IX except phenolphthalein replace methyl-orange as the indicator.

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⁵ This procedure will cause the magma to separate, but inasmuch as it appears impossible with our present processes to produce a magma of the desired strength that will not separate, it seems to the writer that the logical and proper thing is to sacrifice pharmaceutical elegance for uniformity.