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Estimation of Magnesium in Solution of Citrate of Magnesia*

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Since the work of Berg (1) in 1927, the use of 8-hydroxyquinoline, or oxine, as a quantitative precipitant for certain metallic ions, has become definitely established among quantitative analytical procedures. This reagent is especially suitable for the determination of magnesium and the method offers distinct advantages over the classical phosphate procedure.

For the assay of magnesium oxide in Solution of Citrate of Magnesia the Pharmacopœia employs the phosphate method (2). It is believed that this method, even in the considerably simplified form which the Pharmacopœia prescribes, is entirely adequate in accuracy. The liberal limits for the magnesium oxide content (1.6–1.9%) are well within the therapeutic range so that the assay may be regarded to a large extent as a control of the stability of the final preparation. The present study was undertaken to determine the availability of the oxine method for this assay with the realization that the presence of relatively large amounts of sugar and citrate ion would constitute a somewhat special application of the method.

For our preliminary studies we have not attempted to prepare quantitative solutions of the official preparation. We have avoided the obvious difficulties involved in making such preparations by using a simplified solution containing the desired amount of magnesium oxide as magnesium sulfate,

sugar and citric acid. Two of these simplified solutions were prepared representing the limits of magnesium oxide set by the Pharmacopœia, *i. e.*, 1.6% and 1.9%. The sugar and citric acid content of both solutions was the same and in accord with the values prescribed by the Pharmacopœia.

Two methods of procedure for the oxine precipitation were examined. In the first method (3), the slightly acid solution is treated with the required amount of oxine dissolved in acetic acid. The magnesium oxyquinolate is then precipitated by the addition of ammonia. Using this method we found it very difficult to obtain constant weight in the drying of the precipitate.

In the second method (4), the strongly ammoniacal solution, with ammonium chloride added to prevent the precipitation of the magnesium, is treated with the required amount of an alcoholic solution of the oxine. In the subsequent drying of the precipitate, constant weight could be obtained satisfactorily, and this method is therefore the one that was adopted.

For the preparation of the simplified test solutions a reagent grade of the heptahydrate of magnesium sulfate was used and was assayed in the following manner. Approximately 0.5 Gm. of the salt, accurately weighed, was dissolved in 150 cc. of distilled water previously heated to 70° to 80° C. After adding 5 cc. of a 2 *N* solution of ammonium chloride and 3 cc. of stronger ammonia, 14 cc. of a 5% solution of oxine in alcohol was added slowly with stirring. The mixture was allowed to stand for about 30 min. and then the supernatant liquid was decanted through a sintered glass filter crucible. The precipitate was washed four times by decantation with 25-cc. portions of 1% ammonia and then completely transferred to the filter crucible and washed thoroughly with distilled water. The filter crucible and contents were then dried to constant weight at 100–105° C. The results of three determinations gave values of 100.4%, 100.3% and 100.5%, respectively, corresponding to an average value of 100.4% MgSO₄·7H₂O.

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From preliminary experiments with commercial samples of the official Solution of Citrate of Magnesia it was decided to use 2.5 cc. of the solution for the present assay. For a sample of this size the equivalent weight of the magnesium oxyquinolate varies between approximately 345 mg. for a sample containing the equivalent of 1.6% magnesium oxide and 410 mg. for a 1.9% magnesium oxide sample. Subsequent results indicate that magnesium oxyquinolate precipitates within these weight limits could be handled very rapidly and, as will be seen below, with quite satisfactory reproducibility and accuracy in the results.

As indicated above, two simplified magnesium citrate solutions were prepared. Each solution contained 9.4 Gm. of citric acid and 14.6 Gm. of sucrose per 100 cc. of solution. One solution contained an accurately weighed quantity of reagent magnesium sulfate to give approximately the equivalent of 1.6% in magnesium oxide and the other the equivalent of 1.9% magnesium oxide. The actual magnesium oxide equivalents of these solutions after proper correction for the assay of the reagent magnesium sulfate detailed above were 1.61% and 1.90%, respectively.

These two solutions were assayed according to the U. S. P. method and by the oxine method, which was carried out in the following manner. To 150 cc. of distilled water heated to 70–80° C. was added the desired amount of the test solution, followed by 1 cc. of 2 *N* ammonium chloride and 3 cc. of stronger ammonia; 8 cc. of a 5% solution of oxine in alcohol was then added slowly with thorough stirring. After standing approximately 30 min., the supernatant liquid was decanted through a weighed sintered glass filter crucible which had been previously dried at 100–105° C. The precipitate was washed three times by decantation with 20-cc. portions of distilled water and then completely transferred to the filter crucible, followed by thorough washing with distilled water. The filter and contents were dried to constant weight at 100–105° C.

Typical data of assays carried out in triplicate on these solutions are shown in Table I, using the magnesium oxide conversion factor of 0.1157 for magnesium oxyquinolate, $Mg(C_9H_6NO)_2 \cdot 2H_2O$.

It is clear that the results obtained by the oxine method, as employed, are quite satisfactory both in reproducibility and desired accuracy and that therefore the presence of relatively large amounts of sugar and citric acid has no significant effect. These results are consistently lower than those obtained by

the U. S. P. method and agree closely with the calculated values for the magnesium oxide content.

For both the 1.61% and 1.90% solutions the same amount of oxine solution (8 cc.) was used and this amount of the reagent is sufficient to precipitate somewhat more magnesium than corresponds to 1.9% of magnesium oxide, which is the upper limit of the Pharmacopœial standard.

In applying the method to commercial samples of Solution of Citrate of Magnesia we have made one modification in the above method. After removing the excessive carbon dioxide by repeated pouring, exactly 50 cc. of the solution was pipetted into a 100-cc. volumetric flask and diluted to the mark with distilled water. Five cubic centimeters of this diluted solution, a quantity readily handled by a pipette of the conventional transfer type, was used for the assay, and 20 cc. was used for each determination by the U. S. P. method. The 5-cc. pipette and the 20-cc. pipette used throughout the study were checked with reference to the ratio of their delivery capacities, using water as the calibrating medium. This ratio was found to be very close to 1:4 and no correction was necessary for the direct comparison of the results obtained by the two methods.

Commercial samples of Solution of Citrate of Magnesia were purchased from retail druggists in a manner planned to give as wide a representation as possible of the product marketed in this community. Table II gives typical results of the assays, in triplicate, for ten of these commercial preparations.

In regard to the reproducibility of these results there is little choice between the two methods of assay. The oxine method is again found to yield results consistently lower by a few hundredths of a per cent than those obtained by the U. S. P. method. This difference in itself cannot be regarded as of great importance to the present study.

It is interesting to note that of the ten products examined, eight were labeled U. S. P. Of these, only one, sample *B*, falls below the minimum U. S. P. requirement, regardless of which of the two methods, of assay is employed. The label of sample *E* definitely states that the U. S. P. formula has not been followed and neither the label nor cap of sample *F* makes any reference whatever to the Pharmacopœia.

The final evaluation of the two methods rests upon the relative ease of manipulation and the time factor and in these respects the oxine method presents definite advantages. No ignition step is re-

TABLE I

% of MgO Calculated	U. S. P. Method			Oxine Method		
	Gm. of Pyrophosphate	Equivalent MgO in Gm.	% of MgO	Gm. of Oxyquinolate	Equivalent MgO in Gm.	% of MgO
1.61	0.4598	0.1665	1.67	0.3525	0.04078	1.63
	0.4606	0.1668	1.67	0.3514	0.04062	1.62
	0.4595	0.1663	1.66	0.3508	0.04059	1.62
1.90	0.5426	0.1965	1.97	0.4130	0.04778	1.91
	0.5389	0.1951	1.95	0.4146	0.04797	1.92
	0.5381	0.1948	1.95	0.4145	0.04796	1.92

TABLE II

Sample	U. S. P. Method			Oxine Method		
	Gm. of Pyrophosphate	Equivalent MgO in Gm.	% of MgO	Gm. of Oxyquinolate	Equivalent MgO in Gm.	% of MgO
A	0.4423	0.1602	1.60	0.3394	0.03927	1.57
	0.4454	0.1613	1.61	0.3406	0.03941	1.58
	0.4431	0.1604	1.60	0.3413	0.03949	1.58
B	0.4250	0.1539	1.54	0.3296	0.03813	1.53
	0.4272	0.1547	1.55	0.3278	0.03793	1.52
	0.4249	0.1539	1.54	0.3282	0.03797	1.52
C	0.4457	0.1614	1.61	0.3399	0.03933	1.57
	0.4432	0.1605	1.61	0.3405	0.03944	1.58
	0.4461	0.1615	1.62	0.3409	0.03944	1.58
D	0.4652	0.1684	1.68	0.3560	0.04119	1.65
	0.4651	0.1684	1.68	0.3565	0.04125	1.65
	0.4654	0.1685	1.69	0.3564	0.04124	1.65
E	0.3506	0.1270	1.27	0.2690	0.03112	1.24
	0.3493	0.1265	1.27	0.2700	0.03124	1.25
	0.3488	0.1263	1.26	0.2715	0.03141	1.26
F	0.4445	0.1610	1.61	0.3459	0.04002	1.60
	0.4457	0.1614	1.61	0.3436	0.03975	1.59
	0.4467	0.1618	1.62	0.3411	0.03947	1.58
G	0.4472	0.1619	1.62	0.3431	0.03969	1.59
	0.4464	0.1616	1.62	0.3444	0.03985	1.59
	0.4455	0.1613	1.61	0.3439	0.03979	1.59
H	0.4631	0.1677	1.68	0.3528	0.04082	1.63
	0.4645	0.1682	1.68	0.3535	0.04090	1.64
	0.4635	0.1678	1.68	0.3530	0.04084	1.63
J	0.4616	0.1671	1.67	0.3540	0.04096	1.64
	0.4600	0.1666	1.67	0.3522	0.04075	1.63
	0.4611	0.1670	1.67	0.3533	0.04088	1.64
K	0.4552	0.1648	1.65	0.3501	0.04050	1.62
	0.4555	0.1649	1.65	0.3492	0.04040	1.62
	0.4537	0.1643	1.64	0.3509	0.04057	1.62

quired and therefore there is a considerable time saved by the use of sintered glass filter crucibles, which are highly recommended. We have used both the imported and domestic grades. Pyrex crucibles of medium porosity are quite satisfactory.

Magnesium oxyquinolate is highly insoluble in water and is precipitated for the most part in rather large granules which are easily washed and transferred. A limited amount of finely divided material with a tendency to "creep" is usually formed also but this offers no serious difficulty. The unusually low magnesium oxide conversion factor of 0.1157 suggests important advantages.

In the drying of the precipitate to constant weight at 100–105° C. we have met with some disappointment. Contrary to the procedure usually cited in the literature we have found it necessary to heat for 2 hrs. and then for one or two 1/2-hr. periods in order to attain constant weight. It may well be that the admixture of a small amount of sugar with the oxyquinolate precipitate considerably lengthens the drying period.

SUMMARY

1. A procedure for the assay of mag-

nesium oxide in Solution of Citrate of Magnesia based on the oxine method has been described.

2. The results obtained by this procedure on ten commercial preparations of Solution of Citrate of Magnesia have been tabulated and compared with the corresponding results obtained by the U. S. P. method.

3. The oxine method of assay compares favorably with the U. S. P. method in the accuracy and reproducibility of results.

4. The oxine method represents a more simplified and rapid procedure and is therefore recommended.

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