α-Oximino-β-(*p*-nitrophenyl)-propionic Acid.—In a one-litre Erlenmeyer flask was placed a solution of 23.1 Gm. (0.1 mole) of the sodium salt of the quinoid form of *p*-nitrophenylpyruvic acid ethyl ester in 100 cc. of methyl alcohol. To this was added a solution of 13.8 Gm. (0.2 mole) of hydroxylamine hydrochloride and 27.2 Gm. (0.2 mole) of sodium acetate in 300 cc. water. After mixing the two solutions, 10 cc. glacial acetic acid was added with stirring. The reaction mixture became light yellow in color, and the flask was stoppered and allowed to stand for one hour with occasional shaking. The mixture was transferred to a distilling flask, and most of the methyl alcohol was removed at room temperature under reduced pressure. The residual aqueous mixture was cooled overnight, and a flocculent yellow precipitate was formed. The crystals were filtered off and washed with cold water, then dried over sulfuric acid. Pale yellow crystals melting at 161–162° and weighing 22.6 Gm. (90%) were obtained.

Anal.—Calcd. nitrogen for $C_{11}H_{12}O_5N_2$. 11.1%. Found: (Kjeldahl) 11.3%, 11.4%.

p-Aminophenylalanine Ethyl Ester Dihydrochloride.—To 5.2 Gm. (0.021 mole) of α-oximino-β-(*p*-nitrophenyl)-propionic acid ethyl ester dissolved in 100 cc. of 50% alcohol were added 10 cc. 36% hydrochloric acid and 3 Gm. 10% palladium-5% platinum catalyst. The mixture was shaken in hydrogen at a pressure of one atmosphere, and the theoretical quantity of hydrogen, 2300 cc., was absorbed in six hours. The absorption of hydrogen was rapid at first, 1100 cc. being taken up in one hour, but the reduction became much slower as it neared completion. The mixture was filtered to remove the catalyst, and the clear filtrate was transferred to a Claisen flask. The flask and contents were warmed to 60° and the solvents removed at reduced pressure. After evaporation of solvents there remained a residue of faintly yellow crystals. These were redissolved in absolute alcohol and precipitated by the addition of isopropyl ether, then filtered out and dried. Five grams (87%) of the ethyl ester of *p*-aminophenylalanine dihydrochloride was obtained. The crystals were pale yellow and very hygroscopic.

Anal.—Calcd. nitrogen for $C_{11}H_{16}O_2N_2 \cdot 2HCl$: 9.99%. Found: (Kjeldahl) 10.1%, 10.5%.

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Determination of Magnesium in Magnesium Sulfate and Solution of Magnesium Citrate*

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Magnesium Citrate Solution and Magnesium Sulfate were assayed by oxine and by pyrophosphate procedures and the results compared. Precipitation of the magnesium as the oxyquinolate is recommended as the preferred method.

THE proposed new United States Pharmacopœia XIII assay for magnesium oxide in Magnesium Citrate Solution (1) is based on Berg's (2) procedure, using 8-hydroxyquinoline as modified by Bell (3). Fifty cubic centimeters of the Solution are diluted to exactly 100 cc. with water. Five cubic centimeters of this dilution are mixed with 150 cc. of distilled water at 70° to 80°. Then 1 cc. of 2 *N* ammonium chloride and 3 cc. of stronger ammonia are added and mixed, followed by 8 cc. of a 5 per cent solution of oxine in alcohol which is added slowly with constant stirring. After thirty minutes, the precipitate is washed three times by decantation and is collected on a sintered-glass filter crucible, previously dried at 100° to 105° and weighed, washed well with distilled water, and the crucible and contents are dried for two hours at 100° to 105°. The weight of magnesium oxyquinolate multiplied by 4.628 gives the equivalent of magnesium oxide in 100 cc. of the Solution.

In order to check the new method, 21

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commercial samples of Solution of Magnesium Citrate were assayed by the pyrophosphate procedure of the U. S. P. XII (I) and the proposed oxine method (II). The results of the analyses are given in Table I.

These results indicate that the oxine procedure yields results nearer the true values, the average being 99.92%; while the average for the results by the pyrophosphate method is 101.04%.

As a further check on the magnesium sulfate heptahydrate, 9.7941 Gm. of the salt was heated in a muffle at about 420° until no further loss in weight was noted (forty-four hours). The weight of the residual anhydrous magnesium sulfate, 4.7875 Gm., represented 48.88% of the hydrated salt. The theoretical value is 48.84%, indicating the loss of a negligible amount of water of hydration. Anhydrous magnesium sulfate, 8.608 Gm., (prepared as above) was placed in a 250-cc. volumetric flask and distilled water was added to make 250 cc. of solution at 20°. This solution was assayed by the U. S. P. XII procedure for Magnesium Sulfate using 15-cc. ali-

TABLE I

Sample	U. S. P. Method			Oxine Method		
	Gm. of Pyrophosphate	Equiv. MgO in Gm.	% of MgO	Gm. of Oxyquinolate	Equiv. MgO in Gm.	% of MgO
1	0.4307	0.1559	1.56	0.3334	0.03858	1.54
2	0.4383	0.1587	1.59	0.3309	0.03830	1.53
3	0.4653	0.1685	1.69	0.3530	0.04085	1.63
4	0.4447	0.1611	1.61	0.3338	0.03865	1.55
5	0.4499	0.1629	1.63	0.3364	0.03893	1.56
6	0.4496	0.1628	1.63	0.3359	0.03888	1.56
7	0.4477	0.1621	1.62	0.3389	0.03920	1.57
8	0.4543	0.1645	1.65	0.3437	0.03978	1.59
9	0.4210	0.1525	1.53	0.3202	0.03705	1.48
10	0.4431	0.1604	1.60	0.3398	0.03933	1.57
11	0.4558	0.1651	1.65	0.3466	0.04010	1.60
12	0.4489	0.1626	1.63	0.3431	0.03970	1.59
13	0.4431	0.1604	1.60	0.3416	0.03953	1.58
14	0.4417	0.1600	1.60	0.3396	0.03930	1.57
15	0.4426	0.1603	1.60	0.3403	0.03938	1.58
16	0.4590	0.1662	1.66	0.3491	0.04040	1.62
17	0.4249	0.1538	1.54	0.3259	0.03440	1.51
18	0.4921	0.1782	1.78	0.3650	0.04223	1.69
19	0.4294	0.1555	1.56	0.3281	0.03798	1.52
20	0.4372	0.1583	1.58	0.3328	0.03850	1.54
21	0.4386	0.1587	1.59	0.3354	0.03881	1.55

With method I 14 samples met the minimum requirement of 1.60 Gm. of magnesium oxide in 100 cc. of Solution of Magnesium Citrate, while 7 samples fell below the lower limit, only 2 samples dropping below 1.55 Gm. Method II showed only 4 samples meeting the minimum requirement with 6 samples dropping below 1.55 Gm.

According to the above results, method II should not replace method I unless it is shown that the results obtained by method II are in closer agreement with the true values than are those yielded by method I. To investigate this problem, the following experiments were carried out.

TABLE II.—ANALYSES OF MAGNESIUM SULFATE BY U. S. P. AND OXINE METHODS

U. S. P. Method

$MgSO_4 \cdot 7H_2O$ Weighed	Gm. of Pyrophosphate	Equivalent $MgSO_4 \cdot 7H_2O$ in Gm.	% Recovery
1.0873	0.4965	1.0995	101.12
0.9967	0.4547	1.0070	101.03
0.9424	0.4309	0.9543	101.26
1.0658	0.4846	1.0732	100.79
1.0833	0.4943	1.0947	101.05
0.9987	0.4554	1.0085	100.98

Oxine Method

$MgSO_4 \cdot 7H_2O$ Weighed	Gm. of Oxyquinolate	Equivalent $MgSO_4 \cdot 7H_2O$ in Gm.	% Recovery
0.2759	0.3890	0.2750	99.67
0.2597	0.3654	0.2583	99.46
0.3032	0.4274	0.3022	99.67
0.2582	0.3652	0.2582	100.00
0.2710	0.3845	0.2718	100.29
0.2653	0.3769	0.2665	100.45

EXPERIMENTAL

Magnesium sulfate heptahydrate, reagent grade, was analyzed by the U. S. P. XII pyrophosphate procedure and by the above given oxine procedure, with the use of 3 cc. of 2 *N* ammonium chloride instead of 1 cc. The first three oxyquinolate precipitates were heated at 100–105° for one and a half hours and then for three half-hour periods. The next three were heated at 100–105° for one two-hour and two half-hour periods. In both cases constant weight was attained in two hours. The results are given in Table II.

quots, containing 0.5165 Gm. of the anhydrous salt. The oxine procedure was carried out using 5-cc. aliquots, containing 0.1722 Gm. of the anhydrous salt, and using 4 cc. of 2 *N* ammonium chloride and 10 cc. of the 5% oxine reagent. The results of analyses in triplicate were 101.24% recovery by the pyrophosphate method, and 99.55% recovery by the oxine method.

The above results obtained in the analyses of hydrated and anhydrous magnesium sulfate indicate that the pyrophosphate assay for Magnesium Sulfate in the U. S. P. XII should be replaced by the oxine assay. The following procedure is recommended:

Transfer the accurately weighed Magnesium Sulfate obtained in the test for *loss on drying* to a 100-cc. volumetric flask and add water to make 100 cc. of from a burette into 100-cc. volumetric flasks 46.67 cc. and 39.30 cc., containing 5.6723 Gm. of $MgSO_4$ and 4.7765 Gm. of $MgSO_4$ equivalent to 1.90 Gm. of MgO and 1.60 Gm. of MgO, respectively. To each flask were added 9.4 Gm. of citric acid and 14.6 Gm. of sucrose and enough water to make 100 cc. of solution. These two solutions were assayed by the U. S. P. XII method (I) and by the oxine method (II). The oxyquinolate precipitate did not seem to reach a reasonably constant weight in two hours at 100–105° and the heating was continued as indicated in Table III.

The results indicate that the oxyquinolate precipitate and crucible should be heated for at least three hours instead of two hours as stated in the proposed method, and it is recommended that this change be made. The values recorded after heating

TABLE III.—RELATIONSHIP OF RESULTS BY OXINE METHOD TO LENGTH OF HEATING PERIOD

Sample No.	Calculated Gm. of MgO in 100 Cc. of Solution	Results Expressed as Gm. of MgO/100 Cc. and % Recovery — 2 Hr. at 100–105°		2½ Hr. at 100–105°		3 Hr. at 100–105°		3½ Hr. at 100–105°	
1	1.90	1.9077	100.40	1.9067	100.35	1.9035	100.18	1.8998	99.99
2		1.9067	100.35	1.9044	100.23	1.9012	100.06	1.8970	99.84
3		1.8998	99.99	....	....	1.8956	99.77	1.8952	99.75
4		1.8998	99.99	....	....	1.8933	99.65	1.8933	99.65
5		1.9049	100.26	....	....	1.8961	99.79	1.8952	99.75
6		....	....	....	....	1.9095	100.50	1.9086	100.45
7		....	....	....	....	1.9058	100.31	1.9053	100.28
8		....	....	....	....	1.9077	100.40	1.9072	100.38
9	1.60	1.6105	100.66	....	....	1.6078	100.48	1.6064	100.40
10		1.6129	100.80	....	....	1.6096	100.60	1.6082	100.51
11		1.6166	101.04	....	....	1.6092	100.57	1.6073	100.46
12		1.6092	100.57	....	....	1.5999	99.99	1.5967	99.79
13		1.6133	100.83	1.6119	100.75	....	....	1.6018	100.11
14		1.6096	100.60	1.6073	100.46	....	....	1.5957	99.73
15		1.6175	101.09	1.6142	100.89	....	....	1.6013	100.08
16		1.6119	100.75	1.6082	100.51	....	....	1.5925	99.53
17		....	....	....	....	1.5934	99.59	1.5920	99.50
18		....	....	....	....	1.5930	99.56	1.5916	99.47
19		....	....	....	....	1.6004	100.02	1.6004	100.02
Av.			100.56		100.53		100.10		99.98

solution. Transfer exactly 25 cc. of this solution to a beaker containing 130 cc. of water heated to about 80°, add 4 cc. of ammonium chloride T. S. and then 3 cc. of stronger ammonia T. S. Mix thoroughly and add dropwise, with stirring, 8 cc. of 8-hydroxyquinoline T. S. (5% in alcohol). After standing for thirty minutes, pour off the supernatant liquid through a sintered-glass filter crucible, previously dried at 100° to 105° and weighed. Wash the precipitate three times by decantation, and then transfer it completely to the filter and wash thoroughly with water. Dry the crucible and contents for two hours at 100° to 105°, cool, and weigh. The weight of magnesium oxyquinolate, multiplied by 1.381, indicates the equivalent weight of $MgSO_4$ in the weighed sample.

A solution of magnesium sulfate was prepared by transferring 12.154 Gm. of anhydrous salt to a 100-cc. volumetric flask and adding water to make 100 cc. From this solution two simulated solutions of magnesium citrate were prepared by measuring for three hours are used in Table IV showing comparative results of analyses of the simplified magnesium citrate solutions by methods I and II.

The average values of 1.946 Gm. and 1.638 Gm. per 100 cc. obtained by method I are 2.42% and 2.37% above the respective calculated values. The average values of 1.9025 Gm. and 1.6014 Gm. per 100 cc. obtained by method II are 0.13% and 0.09% above the respective calculated values. Bell (3) reported analyses by methods I and II of two standard simplified magnesium citrate solutions, prepared essentially as indicated above. His results by method I were 3.53% and 2.98% above the calculated values; while his results by method II were 0.88% and 0.83% above the calculated values. When the values obtained after heating the oxyquinolate precipitate for two hours are substituted for those in the above table, the average values in the present case by method II are 0.21% and 0.81% above the respective calculated values.

The work here reported is in substantial agreement with the findings of Bell (3) and emphasizes the superiority of the proposed oxine procedure over the pyrophosphate procedure for the determination of magnesium in Solution of Magnesium Citrate. It also indicates that those manufacturers of Solution of Magnesium Citrate who have been aiming successfully at the minimum magnesium oxide content for their preparations will find it necessary to raise their sights slightly to make a product that will meet the minimum requirement when assayed by the proposed method.

TABLE IV

Calculated Gm. of MgO in 100 Cc. of Solution	U. S. P. Method			Oxine Method		
	Gm. of Pyrophosphate	Equivalent MgO in Gm.	MgO in Gm./100 Cc.	Gm. of Oxyquinolate	Equivalent MgO in Gm.	MgO in Gm./100 Cc.
1.90	0.5366	0.1943	1.94	0.4113	0.04759	1.90
	0.5375	0.1946	1.95	0.4108	0.04753	1.90
	0.5375	0.1946	1.95	0.4096	0.04739	1.90
	0.5398	0.1954	1.95	0.4091	0.04733	1.89
	0.5360	0.1941	1.94	0.4097	0.04740	1.90
	....	....	..	0.4126	0.04774	1.91
	....	....	..	0.4118	0.04765	1.91
	....	....	..	0.4122	0.04769	1.91
1.60	0.4522	0.1637	1.64	0.3474	0.04019	1.61
	0.4528	0.1640	1.64	0.3478	0.04024	1.61
	0.4532	0.1641	1.64	0.3477	0.04023	1.61
	0.4533	0.1641	1.64	0.3457	0.04000	1.60
	0.4506	0.1632	1.63	0.3443	0.03984	1.59
	....	....	..	0.3442	0.03982	1.59
	....	....	..	0.3458	0.04001	1.60

SUMMARY

1. Results obtained in the analyses of Magnesium Sulfate and Solution of Magnesium Citrate by oxine procedures have been tabulated and compared with the corresponding results obtained by the U. S. P. methods.

2. The oxine method of assay for magnesium has been shown to be more accurate than the pyrophosphate procedures of the U. S. P. XII for Magnesium Sulfate and Solution of Magnesium Citrate.

3. A procedure for the assay of $MgSO_4$ in Magnesium Sulfate U. S. P. based on the oxine method has been described and is recommended.

4. It has been shown that the oxyquinolate precipitate obtained in the proposed new U. S. P. assay should be heated for a longer period at 100° to 105° than the directed two hours, and that heating for three hours gives more accurate results. This change in the procedure is recommended.

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