The Analysis of Barium Sulfate

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A method suitable for compendial assay of barium sulfate USP has been developed. Barium is separated as the carbonate and precipitated as the chromate. Calcium, strontium, and silica do not interfere. The calcium and strontium content may be determined by atomic absorption or X-ray fluorescence and silica by a colorimetric procedure. An *in vitro* study of the extractability of strontium and lead from barium sulfate into simulated gastric and intestinal fluids was performed.

THE CURRENT USP XVII (1) monograph for barium sulfate does not include an assay procedure. At the suggestion of the USP Committee of Revision, an investigation was initiated and an analytical procedure for the assay of barium sulfate was developed. Norwitz has published methods for the analysis of barium compounds by homogeneous precipitation as barium chromate (2, 3). The procedures were reported to be accurate in the presence of small amounts of strontium and calcium. With some modifications, the Norwitz method has been found satisfactory for the routine assay of barium sulfate. Since the presence of calcium, strontium, and silica was expected, tests for these elements were also developed. The possibility of strontium or lead extraction from barium sulfate was investigated by an *in vitro* experiment.

BARIUM SULFATE ASSAY

Procedure—Weigh accurately between 0.58 and 0.62 g. of sample in a tared platinum crucible. Add 10 g. of anhydrous sodium carbonate and mix by rotating the crucible. Fuse over a Meker burner until a clear melt is obtained and then heat for an additional 30 min. Cool, place the crucible in a 400-ml. beaker, add 250 ml. of distilled water, stir with a glass rod, and heat to dislodge the melt. Remove the crucible from the beaker and wash thoroughly with water, collecting the washings in the beaker. Rinse the inside of the crucible with 2 ml. of 36% acetic acid and then with water, again collecting the washings in the beaker. Continue heating and stirring until the melt is disintegrated. Cool the beaker in an ice bath until the precipitate settles. Decant the clear liquid through a Whatman No. 40 filter paper, taking care to transfer as little precipitate as possible to the paper. Wash twice by decantation as follows: wash down the inside of the beaker with about 10 ml. of cold 2% (w/v) sodium carbonate solution. Swirl the contents of the beaker and allow the precipitate to settle. Decant the supernatant liquid through the same filter paper as before, transferring as little precipitate as possible. Place the beaker containing the bulk of the barium carbonate precipitate under the funnel and wash the filter paper with five 1-ml. portions of 10% hydrochloric acid. Wash the paper well with water. Dilute the solution (which may be slightly hazy) with 100 ml. of distilled water, and then add 5.0 ml. of hydrochloric acid, 10.0 ml. of 40% (w/v) ammonium acetate solution, 25 ml. of 10% (w/v) potassium dichromate solution, and 10.0 g. of urea. Cover the beaker with a watch glass (not ribbed) and digest on the steam bath, or at 80–85°, for at least 16 hr. Filter while hot through a tared *fine* porosity sintered-glass crucible. Scrub the beaker several times with a rubber policeman to insure that all the precipitate is removed from the beaker. Wash with 0.5% (w/v) potassium dichromate solution and finally with about 20 ml. of water. Dry for 2 hr. at 105°, cool, and weigh.

$$\% \ BaSO_4 = \frac{\text{wt. } BaCrO_4 \times 0.9213 \times 100}{\text{sample wt.}}$$

Results and Discussion—In the procedure initially developed, the precipitation was performed by boiling on a hot plate for 1 hr. after a precipitate first appeared. When the method was put into routine use, some difficulties were encountered. Results were not always reproducible and samples were frequently lost due to "bumping" as the precipitate that formed began to settle. The procedure was modified to that given above in which precipitation is carried out by digestion at 80–85° overnight. No difficulties have since been encountered. Replicate results on various samples are listed in Table I.

A very small amount of barium sulfate is reprecipitated with the barium carbonate. This is not dissolved by the hydrochloric acid used to dissolve the barium carbonate, and if it is transferred to the filter paper it will be lost. However, if the barium carbonate is washed by decantation, as directed, a negligible amount of barium is lost. An ignition of a filter paper from the decantation procedure showed less than 0.05% residue based on the initial sample weight. Any barium sulfate remaining in the sample solution will be filtered off and weighed as barium chromate in the final step of the procedure. It was found that the final barium chromate precipitate contains less than 0.5% barium sulfate. This has a negligible effect on the assay result be-

TABLE I—BARIUM SULFATE ASSAY

Sample	Results, %
Ref. Std. laboratory prepared	99.79, 100.06, 100.11, 99.90, 100.09
1	98.57, 98.39, 98.36, 98.49
2	98.40, 98.30, 98.07, 98.22
314	98.23, 98.43, 98.44, 98.57
316	98.49, 98.70, 98.55, 98.74

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cause of the small difference in molecular weights of barium sulfate and barium chromate.

An experiment using ^{133}Ba tracer showed about 0.04% of the total barium was lost in the sodium carbonate filtrate, and about 0.06% was lost in the chromate filtrate. Atomic absorption analysis for barium in the chromate filtrate also showed less than a 0.1% loss of barium. Thus total barium losses were found to be about 0.1%.

Calcium and strontium present in barium sulfate do not interfere with the assay since they do not precipitate. Atomic absorption analysis showed that less than 0.05% of the weight of the final barium chromate precipitate is due to calcium and strontium chromates. It was suggested[1] that the ability of the method to separate calcium and strontium at high levels be evaluated. A synthetic "low assay" mixture was prepared containing 70% barium sulfate, 20% strontium sulfate, and 10% calcium sulfate. This mixture was submitted for routine assay by the procedure given above. Duplicate results obtained were 71.6% and 70.6% $BaSO_4$. The slightly high and relatively imprecise results obtained on this mixture may have been due to coprecipitation of calcium and strontium. However, this experiment did demonstrate that essentially barium content is measured.

Other Methods Investigated—As a check of the proposed method, an alternate assay method was developed. The sample was fused with sodium carbonate as in the proposed procedure above. After dissolving the barium carbonate in hydrochloric acid, a slight excess of standardized EDTA solution was added and the pH adjusted to about 10. The excess EDTA was back titrated with magnesium chloride using Eriochrome Black T indicator. In this method, calcium and strontium were also quantitatively titrated. These elements were determined by atomic absorption and the assay corrected for their content. The corrected EDTA results showed about the same precision as the chromate assays and the averages of 10 determinations by each method differed by 0.05%.

DETERMINATION OF SILICA

Procedure—Transfer 0.5 g. of sample to a platinum crucible. Add 5 g. of anhydrous sodium carbonate. Heat over a Meker burner with occasional gentle swirling until the melt is clear and continue heating for an additional 30 min. Cool, rinse the outside of the crucible, and place it in a 250-ml. plastic beaker. Add 100 ml. of water and heat on the steam bath with frequent stirring for 1 hr. Cool to room temperature. Rinse and remove the crucible. Filter through Whatman No. 42 filter paper into a plastic beaker and wash the precipitate and paper thoroughly. Prepare a blank by dissolving 5 g. of sodium carbonate in about 100 ml. of water and carry through the remainder of the procedure. Add to the filtrate 15 ml. of 6 *N* sulfuric acid. Adjust the pH to 4.5–5.0 with 6 *N* sulfuric or silica-free ammonium hydroxide if necessary. Heat on a steam bath to dispel carbon dioxide. Cool to room temperature, transfer to a 200-ml. volumetric flask, and dilute to volume with water. Determine the silica colorimetrically as the reduced silicomolybdate complex as given by Boltz (4), using a 10-ml. aliquot of the solution.

[1] Personal communication, Dr. E. F. Salim, Drug Standards Laboratory.

Results and Discussion—Fusion with sodium carbonate is the method commonly used in analyses of silica-containing materials and was found amenable to barium sulfate. However, the 30-min. fusion time is necessary to convert all of the silica to a soluble form. Samples fused only until the melt was clear gave results which were low and nonreproducible. Fusion times of more than 30 min. were not found to be necessary.

The following experiments were performed to check for losses of silica. The barium carbonate precipitate was checked for silica content on four replicates of a selected high silica sample which averaged 0.83%. The barium carbonate precipitate was dissolved in acid and tested by the colorimetric procedure. The amounts of silica found were 0.02, 0.02, 0.04, and 0.05% on the total sample basis. No silica was found on the filter paper after dissolution of the barium carbonate. This was checked by igniting the paper, fusing the residue with sodium carbonate, and testing for silica colorimetrically.

Silica in solution sometimes polymerizes and in some forms will not form the molybdate complex. Two of the solutions remaining after taking aliquots for the colorimetric determination were tested for silica gravimetrically. The results agreed with those obtained colorimetrically, indicating that all silica in the solution was in a complexable form.

DETERMINATION OF CALCIUM AND STRONTIUM

Procedure—Weigh 0.25 g. of sample into a 150-ml. beaker and add 5 ml. of 70% perchloric acid. Cover with a watch glass and heat on a hot plate until dissolved (15–30 min.). A trace of silica may remain. Cool, wash down the watch glass and sides of the beaker with a small amount of water. The barium sulfate will reprecipitate. Add 50 ml. of 0.1 *M* EDTA solution and adjust the pH to about 10 with 20% sodium hydroxide solution. Cover with a watch glass and boil to redissolve (about 30 min.). Cool, transfer quantitatively to a 100-ml. volumetric flask, and dilute to volume with water. Prepare a reagent blank and carry it through the entire procedure. Determine the calcium and strontium content of these solutions by atomic absorption spectrophotometry using the standard addition-extrapolation technique. Calculate the percent calcium sulfate and strontium sulfate in the sample.

Alternately, the samples can be compared with known mixtures of $BaSO_4$, $CaSO_4$, and $SrSO_4$ by X-ray fluorescence. The two methods were found to give equivalent results.

COMPOSITION OF BARIUM SULFATE USP

Qualitative spectrographic analysis indicated only trace contamination by other cations except sodium and potassium. It is estimated that their combined concentration is less than 0.1%. The composition of barium sulfate indicated by these analyses is summarized in Table II.

THE *IN VITRO* EXTRACTION OF STRONTIUM AND LEAD

The only potentially hazardous substances encountered in this study were strontium and lead. Tests were conducted with simulated gastric and

TABLE II—SUMMARY OF RESULTS, %[a]

Sample	Assay	$SrSO_4$	$CaSO_4$	SiO_2	Loss on Ignition 1,000°C.	Total
1	98.45	0.89	0.36	0.16	0.20	100.06
2	98.20	0.96	0.46	0.16	0.20	99.98
314	98.42	0.88	0.36	0.19	0.15	100.00
316	98.62	0.92	0.29	0.12	0.16	100.11
Precision[b]	±0.32	±0.05	±0.08	±0.04	—	—

[a] Each value reported is the average of four determinations except the loss on ignition which is a single determination.
[b] Percent absolute, single determination, 95% confidence level.

TABLE III—EXTRACTION OF $BaSO_4$ WITH SIMULATED GASTRIC FLUID AND INTESTINAL FLUID—10-g. $BaSO_4$, 30-ml. FLUID, 37°C., 29 R.P.M.

Sample	Hr. Extracted with Gastric Fluid	Hr. Extracted with Intestinal Fluid	p.p.m. Extracted on a $BaSO_4$ Basis, Atomic Absorption Pb	Sr
25	4	—	<1	—
25	—	4	<1	—
25	8	—	<1	—
25	—	8	<1	—
25	24	—	<1	—
25	—	24	<1	—
25	4 additional	16	<1	—
32	24	—	<1	14
32	—	24	<1	0.9
72	24	—	<1	9
72	—	24	<1	1
112	24	—	<1	13
112	—	24	<1	2
21	24	—	<1	10
21	—	24	<1	2
26	24	—	<1	6
26	—	24	<1	0.6
26 plus 1,000 p.p.m. Pb	24	—	<1	8
26 plus 1,000 p.p.m. Pb	—	24	<1	0.9

intestinal fluids T.S. (5) to determine to what extent these elements were extracted from barium sulfate.

Procedure—Ten-gram samples of barium sulfate were placed in 50-ml. bottles with 30 ml. of simulated gastric or intestinal fluids. The bottles were rotated at 29 r.p.m. in a 37° water bath for various periods of time. The mixtures were centrifuged and filtered. The filtrates were tested for lead and strontium by atomic absorption. Standards were prepared with the simulated fluids to provide a constant matrix.

Results—Six different samples of barium sulfate having total lead contents ranging from 15 to 70 p.p.m. were treated by the above procedure using both fluids and extraction times from 2 to 24 hr. Results on all samples showed less than 1 p.p.m. lead (calculated on $BaSO_4$ basis) extracted into the gastric or the intestinal fluids as shown in Table III. As a further check, one sample was spiked with 1,000 p.p.m. lead (on the $BaSO_4$ basis) and carried through the procedure. Again, less than 1 p.p.m. lead was found. The removal of lead from the fluids in this experiment probably is due to adsorption and precipitation since an excess of sulfate is always present in barium sulfate USP.

Fluids from five of the samples were analyzed for strontium by atomic absorption. The strontium extracted into the fluids (in p.p.m. Sr on the $BaSO_4$ basis) is listed in Table III. The extracted residues contained 0.39–0.60% strontium. These results indicate only slight dissolution of strontium in either of the simulated fluids.

SUMMARY

A procedure has been developed for the assay of barium sulfate for compendial use. Replicate analyses in our laboratory on 52 samples indicate a precision of ±0.32% for a single determination at the 95% confidence level. It is felt that the composition of barium sulfate USP has been characterized by this study. *In vitro* studies indicate that no appreciable quantitites of strontium or lead are extracted from barium sulfate by simulated gastric or intestinal fluids.

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Keyphrases

Barium sulfate—analysis
Gravimetric analysis—barium chromate precipitation
Titrimetric analysis—EDTA, $MgCl_2$
Colorimetric analysis—silica
Atomic absorption spectrometry—calcium, strontium analysis
Strontium, lead extraction—gastrointestinal fluids