Selective Assay of Benzoyl Peroxide in Lotions and Creams

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Abstract □ A selective titrimetric method for the determination of benzoyl peroxide in lotions and creams was developed. It is based on the work of Horner and Jürgens, in which diacylperoxides, dialkylperoxides, peracids, and alkylhydroperoxides can be determined selectively by iodometry and acidimetry. The proposed assay is stability indicating with respect to peracids. Good recovery data were obtained.

Keyphrases □ Benzoyl peroxide—titrimetric, TLC, and spectrophotometric analyses compared, lotions and creams □ Titrimetric analysis—benzoyl peroxide in lotions and creams, compared to TLC and spectrophotometric analyses □ TLC—analysis, benzoyl peroxide in lotions and creams, compared to titrimetric and spectrophotometric analyses □ Spectrophotometric analysis—benzoyl peroxide in lotions and creams, compared to titrimetric and TLC analyses

Gruber and Klein (1) reported that the iodometric titration generally used for the assay of benzoyl peroxide and its pharmaceutical preparations is nonspecific. They proposed a spectrophotometric method based on the measurement of iodine liberated by the oxidation of iodide ion by benzoyl peroxide, and they compared the spectrophotometric and titrimetric procedures with a polarographic assay for benzoyl peroxide. In this laboratory, the Gruber and Klein (1) spectrophotometric assay provides essentially the same results as the titrimetric method, a finding that is not surprising in view of the identity of the chemistry of both methods. Moreover, the polarographic method used by Gruber and Klein (1) could not be reproduced in this laboratory.

Horner and Jürgens (2) described an assay scheme wherein diacylperoxides, dialkylperoxides, peracids, and alkylhydroperoxides can be determined by iodometry and acidimetry with the aid of phenyl sulfide and triethylarsine. Because the simple formulations investigated would not be expected to contain any alkylhydroperoxides or dialkylperoxides, a procedure was developed, based on the Horner and Jürgens work (2), which is selective for benzoyl peroxide in the presence of perbenzoic acid. The procedure is a simple modification of the presently used iodometric titration, requiring only the addition of phenyl sulfide before titration to destroy any perbenzoic acid present.

Table I—Rate of Destruction of Perbenzoic Acid by Phenyl Sulfide

Minutes after Addition	Milligrams Found as Benzoyl Peroxide
0	11.2
2	0
4	0
6	0
8	0
10	0

Table II—Effect of Phenyl Sulfide on Benzoyl Peroxide

Minutes after Addition	Milligrams Taken	Milligrams Found	Percent Recovery
0	24.0	23.4	97.5
3	24.0	22.9	95.5
5	24.0	22.9	95.5
10	24.0	22.9	95.5

The proposed assay was compared with the titrimetric method, the Gruber and Klein spectrophotometric assay (1), and a quantitative thin-layer method. The proposed selective titrimetric method gave results comparable to quantitative TLC values. The modified procedure is presented and the results obtained in the assay of benzoyl peroxide formulations are described in this report.

EXPERIMENTAL[1]

Equipment and Supplies—Phenyl sulfide[2], acetone, sodium thiosulfate, potassium iodide, benzene (all ACS grade or equivalent), and silica gel GF plates[3] (20 × 20 cm, 250 μm) were used.

Quantitative TLC—*Standard Preparation*—Dissolve 250 mg of recrystallized benzoyl peroxide, accurately weighed, in exactly 50 ml of acetone.

Assay Preparation—Transfer a quantity of lotion or cream equivalent to about 250 mg of benzoyl peroxide, accurately weighed, to a 50-ml volumetric flask. Dissolve in, or uniformly disperse in, 30 ml of acetone and dilute to volume with acetone.

Procedure—Streak 0.5 ml (5 × 100 μl followed by a 100-μl rinse of the micropipet with acetone) of the assay preparation and the standard preparation on separate silica gel GF_{254} plates (20 × 20 cm, 250 μm), which had been previously activated for 15–30 min at 105° and which had been prechromatographed in the developing solvent. Develop the plates in a standard unequilibrated chromatography tank (27 × 7 × 28 cm) to within 2–3 cm of the top, employing benzene as the developing solvent.

Locate the benzoyl peroxide streak under shortwave UV light, scrape the streak off, and transfer it into a 125-ml conical flask through a powder funnel. Quantitatively rinse the funnel with 30 ml of acetone. Stir the mixture for about 5 min with a magnetic stirrer and filter quantitatively[4] into a 100-ml beaker, rinsing the flask and funnel with 4 × 5 ml of acetone.

Add 5 ml of a 20% solution of potassium iodide to the filtrate, cover with a watch glass, and place in the dark for about 5 min. Then titrate the liberated iodine against a white background with

[1] Spectrophotometric assays were carried out in a Beckman DU fitted with the Gilford model 222 photometer.
[2] Catalog No. 619, Eastman.
[3] Brinkmann.
[4] Whatman No. 1 filter paper or equivalent.

Table III—Assay for Benzoyl Peroxide in Commercial[a] Products by Four Methods

Sample	Lot	Benzoyl Peroxide, %				
		Claimed	Titrimetric	Spectrophotometric	Proposed	Quantitative TLC
Acne lotion	A	5.0	5.03, 5.16, 4.87	5.02, 5.06	4.34, 4.24, 4.26	4.3
Cream	A	5.0	5.10, 5.09, 5.20	5.40, 5.38	4.91, 4.95, 4.90	3.6
Sulfur cream	A	10.0	10.5, 10.4, 10.5	11.2, 11.2	9.81, 9.67, 9.67	10.5
Cream	B	5.0	4.23, 4.12, 4.15	4.28, 4.25	3.97, 3.99, 3.97	4.4
Cream	C	5.0	5.24, 5.27, 5.26	5.51, 5.53	4.92, 4.85, 4.84	4.9
Lotion	B	5.0	5.30, 5.42, 5.20	5.61, 5.52	4.72, 4.72, 4.70	4.7
Lotion	C	5.0	5.60, 5.60, 5.60	5.69, 5.73	4.52, 4.52, 4.52	4.5

[a] Persadox lotion or cream, Texas Pharmacal Co.

0.01 *N* sodium thiosulfate from a 5-ml buret to the disappearance of the yellow iodine color. Calculate the percent benzoyl peroxide with:

$$\% \text{ benzoyl peroxide} = \frac{\text{ml thiosulfate (assay preparation)}}{\text{ml thiosulfate (standard preparation)}} \times \frac{\text{concentration of standard (g/50 ml)}}{\text{sample weight (g)}} \times 100 \quad \text{(Eq. 1)}$$

Selective Titrimetric Method—*Assay Preparation*—Accurately weigh a sample of cream or lotion equivalent to about 250 mg of benzoyl peroxide into a 100-ml beaker. Add 30 ml of acetone and stir the mixture until a solution or uniform dispersion results. Quantitatively transfer the mixture to a 100-ml volumetric flask with the aid of at least 4 × 10 ml of acetone. Then dilute the mixture to volume with acetone.

Procedure—Transfer 10.0 ml of the assay preparation to a 125-ml glass-stoppered conical flask, add 0.2 ml of phenyl sulfide, and let stand for 4 min. Add 2 ml of a 20% potassium iodide solution and let stand, protected from light, for 15 min. Add 25 ml of acetone and titrate the liberated iodine against a white background with standard 0.01 *N* sodium thiosulfate to the disappearance of the yellow color. Each milliliter of 0.01 *N* sodium thiosulfate is equivalent to 1.211 mg of benzoyl peroxide.

RESULTS AND DISCUSSION

To validate the method, perbenzoic acid was synthesized according to a literature method (3). A solution of perbenzoic acid in chloroform thus obtained, containing 610 mg/ml, was diluted to represent a concentration equivalent in iodide-oxidizing capacity to about 10 mg of benzoyl peroxide/sample aliquot. Samples were assayed at various time intervals after the addition of 0.2 ml of phenyl sulfide (Table I).

The effect of phenyl sulfide on benzoyl peroxide was found to be minimal (Table II). The reduction in assay value after addition of phenyl sulfide may be attributable to the presence of some perbenzoic acid in the sample employed.

Mixtures of benzoyl peroxide with perbenzoic acid were prepared to contain 90.0 and 50.0% of the labeled amount of benzoyl peroxide. Assays of these samples by the proposed method provided results of 90.1 and 50.2%, respectively, as the average of triplicate determinations.

Results of assays of commercial products by the proposed method, a quantitative TLC method, the titrimetric method (same as proposed method without phenyl sulfide), and the Gruber and Klein spectrophotometric method (1) are presented in Table III. A standard of recrystallized benzoyl peroxide, mp 104.8–105.5°, was used in the quantitative TLC method.

Results obtained by the proposed procedure on commercial products were in fair agreement with those obtained by TLC and, in every case, were lower than those obtained by the titrimetric or spectrophotometric method (1). Results obtained by the spectrophotometric method (1) are in good agreement with those obtained by the titrimetric method.

The proposed method is also applicable to the determination of purity of benzoyl peroxide raw materials.

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