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Determination of selenium sulfide using 1,3-dibromo-5,5-dimethylhydantoin (DBH) Analytical methods of pharmacopeias with DBH in respect to environmental and economical concern Part 11☆

Manfred Hilp *

Institut für Pharmazeutische Chemie der Philipps-Universität, Marbacher Weg 6, D-35032 Marburg, Germany

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Abstract

USP 2000 (The United States Pharmacopeia, Rockville, MD, 24th ed., 2000, pp. 1514–1515) and PH. EUR. 1997 (European Pharmacopoeia, 3rd ed., Council of Europe, Strasbourg, 1997, p. 1459) dissolve selenium sulfide by boiling with fuming nitric acid for about 1 h. After cooling to room temperature and dilution with water nitrous acid and nitrogen oxides are removed with urea also by boiling before the iodometric titration is performed. This method can be importantly simplified and improved, when using 1,3-dibromo-5,5-dimethylhydantoin (DBH) in glacial acetic acid in presence of solid potassium bromide. Selenium sulfide is dissolved during 5–10 min at room temperature. The excess of DBH and bromine can be removed with 5-sulfosalicylic acid also without boiling. The point of the indicator change for the iodometric titration is improved in comparison to the method of the pharmacopeias, because the colloidal solution of selenium mostly coagulates. Also the sulfur content of selenium sulfide can be determined with DBH.

Keywords: 1,3-Dibromo-5,5-dimethylhydantoin; 1,3-Dibromo-5,5-dimethyl-2,4-imidazolidinedione [77-48-5]; Selenium sulfide [7488-56-4]

1. Introduction

Selenium sulfide serves as antiseborrheic drug. The formula SeS_2 only describes the atomic relation between selenium and sulfur in the preparation [1]. Se_x–S_y-chains of various length or rings of various size (Se_m–S_n; $m+n=6$, 7, 8 or 12) have been detected [1,2]. Selenium sulfide is not a product with fixed composition. The complex nature depends on the manufacturing process. The

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* Tel.: +49-6421-282-5814; fax: +49-6421-282-6652.
E-mail address: hilp@mailer.uni-marburg.de (M. Hilp).

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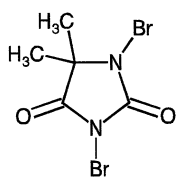
product can be obtained by melting of selenium and sulfur or by reduction of selenious acid with hydrogen sulfide.

To determine the selenium content USP 2000 [3] as well as PH. EUR. 1997 [4] (Fig. 1) heat selenium sulfide on a boiling water bath with 100% fuming nitric acid for 1 h. Selenious acid and sulfuric acid are formed. At room temperature fuming nitric acid does not dissolve selenium sulfide [5]. The arising nitrous acid and the nitrogen oxides, which oxidize iodide to iodine and disturb intensely [6], are removed by boiling with urea. The formed selenious acid is reduced with potassium iodide to red colloidal selenium. The eliminated iodine is titrated with sodium thiosulfate. At the beginning of the titration starch solution must be added in high concentration. The indicator change from brown to red can be recognized more difficultly than in usual iodometric determinations.

The aim of the investigations is to improve the determination of the pharmacopeias for the pure substance of the antiseborrheic drug selenium sulfide using DBH.



DBH is in contrast to elemental bromine and fuming nitric acid a stable and easy to handle crystalline compound [8–17]. DBH has been qualified for the determination of iodide [8,10,11], iodine values [8,15], phenol, resorcinol [8,14], propylthiouracil [8,16], the iodine content of organic compounds according to Schöniger [8,9] and identification tests of PH. EUR. 1997 [8,12,13,17].

2. Experimental

2.1. Materials

Acetic acid [64-19-7] min. 99.8% p.a., Riedel-de Haën art. 33209 = HAc; 1,3-dibromo-5,5-dimethylhydantoin = 1,3-dibromo-5,5-dimethyl-2,4-imidazolidinedione [77-48-5], for synthesis Merck art. 803600 = DBH (for analytical purpose qualified); nitric acid, fuming 100%, [7697-37-2], extra pure, Merck art. 100450; potassium bromide [7758-02-3] extra pure, Merck art. 4900; potassium iodate [7758-05-6] p.a., volumetric standard, Merck art. 5053; potassium iodide [7681-11-0] $\geq$ 99.5%, p.a., Roth, D-76185 Karlsruhe, art. 6750; selenium sulfide, PH. EUR. 1997, USP 2000 [7488-56-4], Galderma; sodium acetate anhydrous [127-09-3] = NaAc, p.a., Merck art. 106268; sodium hydroxide, Rotipuran 99% [1310-73-2], Roth, art. 9356; sodium thiosulfate pentahydrate [7772-98-7] > 98.5%, Roth art. 8649; starch soluble [9005-84-9] extra pure, Merck art. 101253; 5-sulfosalicylic acid dihydrate [5965-83-3], extra pure, Merck art. 689 = SSS; urea [57-13-6], extra pure, Merck art. 108486

2.2. Solutions

DBH–HAc (0.05 M)—1.43 g (0.005 mol) of DBH are dissolved with stirring in glacial acetic acid to 100.0 ml; 0.05 M DBH–0.5 M NaOH—

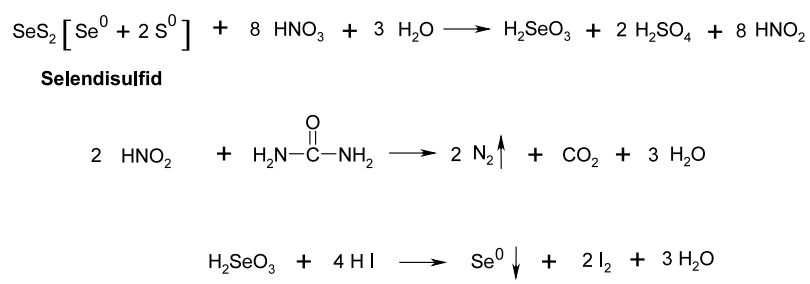


Fig. 1. Determination of selenium sulfide according to USP 2000 and PH. EUR. 1997.

1.43 g (0.005 mol) of DBH are dissolved with stirring in 0.5 M NaOH to 100.0 ml; 1/60 M KIO_3—3.567 g of potassium iodate p.a., volumetric standard, are diluted to 1000.0 ml; 0.25 M NaAc/10 M HAc, pH-buffer about 3.0—20.5 g of anhydrous sodium acetate are dissolved in 570 ml of glacial acetic acid and diluted to 1000.0 ml with water; 0.1 M $Na_2S_2O_3$ is prepared according to PH. EUR. 1997 and standardized with 20.00 ml of 1/60 M KIO_3, 10.0 ml of 0.25 M NaAc/10 M HAc, 5.0 ml of 1 M KI and 0.5 ml of starch solution, iodide-free (PH. EUR. 1997); Starch solution, iodide-free PH. EUR. 1997, without HgI_2, is stable at a temperature of about 4 °C for about 6 weeks. It is necessary to avoid a temperature below 0 °C; 0.2 M SSS: 5.08 g (0.02 mol) of 5-sulfosalicylic acid dihydrate are dissolved in water to 100 ml.

2.3. Assays

2.3.1. Selenium sulfide

2.3.1.1. Determination of the selenium content using DBH/HAc. About 43 mg (0.3 mmol) of selenium sulfide, accurately weighed, are dissolved in 50 ml of 0.05 M DBH–Hac. About 60 mg (~ 0.5 mmol) of solid potassium bromide is added and stirred during 10 min at room temperature. Fifty milliliters of H_2O and 10 ml of 0.2 M SSS are added to the orange colored solution, whose color changes at first to pale yellow and after 1 min disappears completely. Five milliliters of 1 M KI are added after a waiting period of 5 min and the eliminated iodine is titrated after further 5 min and under protection from light with 0.1 M $Na_2S_2O_3$. Starch solution (2.5 ml), iodide-free PH. EUR. 1997 are added at the beginning of the titration. The indicator changes from brown to red. The red elemental colloidal selenium coagulates partly.

1 ml of 0.1 M $Na_2S_2O_3$ is equivalent to 1.974 mg of Se

Weight of sample: 41.42–43.71 mg

USP 2000; PH. EUR. 1997: 52.0–55.5% Se

Found: $n = 7$; $\bar{x} = 53.1$, $s_{rel} = 0.32\%$

2.3.1.2. Determination of blank values. Consumption—0.895 ml of 0.1 M $Na_2S_2O_3$.

2.3.1.3. Determination of blank values with addition of potassium bromide solution. Twenty-five milliliters of 0.05 M DBH–HAc, 25 ml of glacial acetic acid, 50 ml of 0.07 M KBr, 10 ml of 0.2 M SSS are mixed. After 5 min 5 ml of 1 M KI are added. Iodine is not eliminated.

Consumption—0.000 ml of 0.1 M $Na_2S_2O_3$.

2.3.1.4. Determination of selenium content according to PH. EUR. 1997. Weight of sample: 98.96–103.2 mg; USP 2000; PH. EUR. 1997: 52.0–55.5%; Se found: $n = 7$; $\bar{x} = 53.3$, $s_{rel} = 0.56\%$. Comparison to Section 2.3.1.1: F-test $\alpha = 0.19$; t-test, two-sided, $\alpha = 0.13$.

2.3.1.5. Determination of the sulfur content. About 24.3 mg (0.17 mmol) of selenium sulfide, accurately weighed, are dissolved in 25.00 ml of 0.05 M DBH–HAc with addition of about 60 mg of solid KBr and stirring during 10 min at room temperature. Fifty milliliters of H_2O are added to the red colored solution by moistening at first the border of the flask. Then the stopper of the flask is opened only to such a degree, that H_2O is soaked in preferably between the stopper and the grinding. Bromine vapor is not allowed to escape. The color of the solution changes to a dark yellow. Shake vigorously to absorb the bromine vapors. Five milliliters of 1 M KI are added in exactly the same manner as the water has been inserted. Afterwards, the stopper, the grindings and the walls of the flask are rinsed with 10 ml of H_2O. The liberated iodine is titrated under light protection with 0.1 M $Na_2S_2O_3$ after a waiting period of 5 min. Starch solution (2.5 ml), iodide-free PH. EUR. 1997 are added at the beginning of the titration. The change of the indicator occurs from brown to red. After a further waiting period of 15 min under light protection the meanwhile eliminated iodine is titrated again.

Blank value: the mixture of 25.0 ml of H_2O, 25.00 ml of 0.05 M DBH–HAc, 5 ml of 1 M KI is titrated with 0.1 M $Na_2S_2O_3$. Starch solution (0.5 ml), iodide-free PH. EUR. 1997, are added at the beginning of the titration.

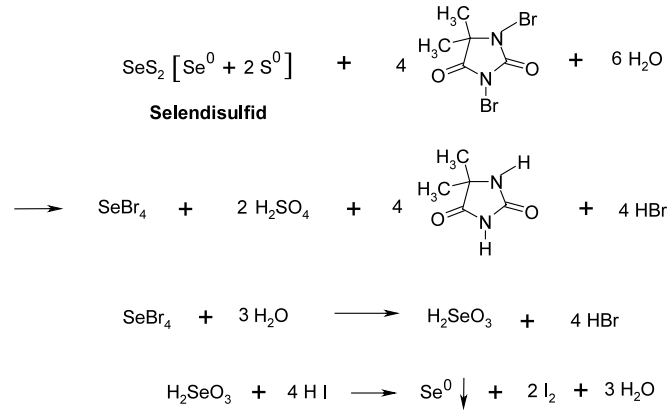


Fig. 2. Determination of selenium in selenium sulfide using DBH.

1 ml of 0.1 M $Na_2S_2O_3$ [difference of blank value − analytical value] is equivalent to 0.5343 mg of S
Weight of sample: 23.63–24.53 mg
Calculated: 46.9% S (100–53.1 [found selenium content])
Found: $n = 7$; $\bar{x} = 46.4\%$ S; m.A. $= -1.1\%$; $s_{rel} = 1.35\%$

2.4. Statistical methods

Evaluations and graphics have been performed with Excel 97 on an IBM-compatible PC running under Windows 95. The built-in *F*- and *t*-test routines of Excel 97 have been used.

3. Results and discussion

3.1. Determination of the selenium content in selenium sulfide using DBH

Selenium [7,18] as well as selenium sulfide [5] react with bromine (Fig. 2). DBH–HAc is able to oxidize selenium sulfide at room temperature in contrast to fuming nitric acid, whereby an orange colored solution arises. The analyte dissolves immediately with a violent development of bromine vapors, when heated for a short time. As shown in Fig. 3, the dissolution at room temperature is strongly accelerated, if solid potassium bromide is added. The oxidation is already finished after 5–10 min without a remarkable liberation of bromine vapors. No different results are obtained when adding 0.3–4 mmol of solid potassium bromide (see Table 1).

Sulfosalicylic acid [8–11,19,20] can remove the excess of DBH after the addition of H_2O also without boiling. The recognition of the indicator change is improved in comparison to USP and PH. EUR. 1997, because the colloidal solution of selenium almost coagulates.

A potentiometric indication is impossible, because elemental selenium precipitates at the diaphragm of the measuring electrode.

Fifty milliliters of 0.05 M DBH–HAc are sufficient for a weight of sample up to about 57 mg (~ 0.4 mmol).

Significantly different results with DBH–HAc (RSD = 0.32) are not obtained in comparison to PH. EUR. 1997 (RSD = 0.56, *F*-test $\alpha = 0.19$; *t*-test, two-sided, $\alpha = 0.13$).

3.2. Determination of blank values

PH. EUR. 97 prescribes the determination of a blank value in order to take into account traces of nitrous acid and nitrogen oxide, which are not decomposed by urea. High blank values of about 8% concerning the analytical value of selenium sulfide are obtained, if DBH–HAc is used with addition of only solid potassium bromide. High concentrations of hydrobromic acid arise during the reaction of selenium sulfide with DBH. If the

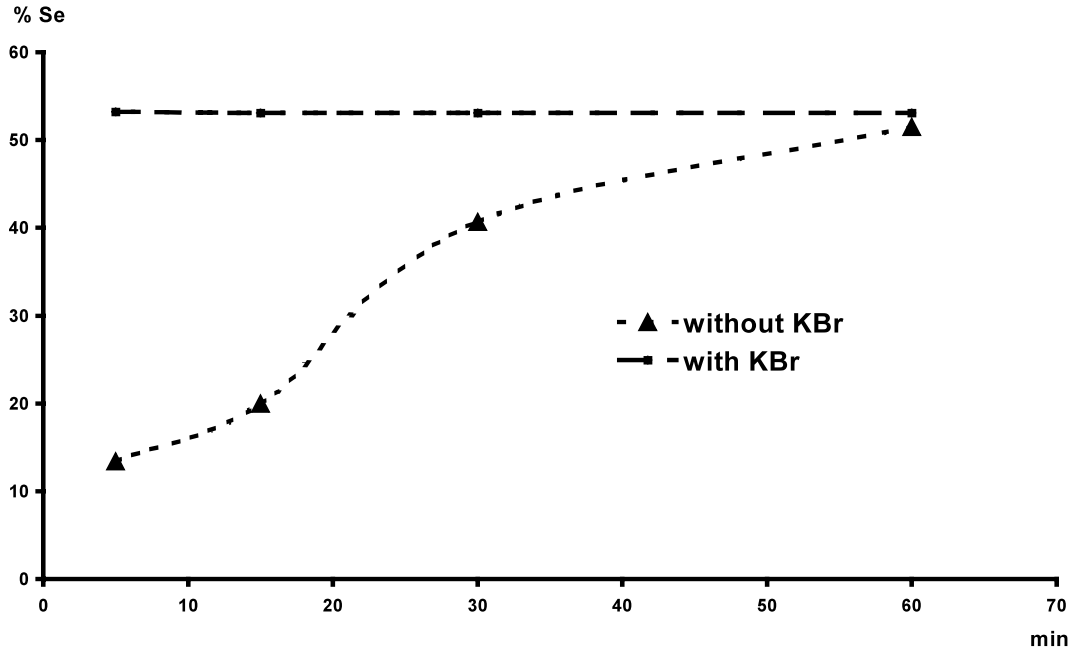


Fig. 3. Dissolution of selenium sulfide depending on time and the addition of about 1 mmol of solid potassium bromide.

Table 1
Determination of the selenium content in selenium sulfide using 0.05 M DBH/HAc, various waiting times, various additions of solid sodium bromide and various weights of sample

Weight of sample (mg)	Addition of sodium bromide (mg)	Waiting time for dissolution of SeS_2 (min)	% Selenium
42.93	–	5	13.4
43.35	–	15	20.0
42.72	–	30	40.7
43.17	–	60	51.5
42.89	119	5	53.2
41.79	119	15	53.1
41.42	119	30	53.1
43.31	119	60	53.1
43.39	29.8	10	50.6
42.81	39.7	10	53.6
41.28	59.5	10	53.1
43.71	515	5	53.0
43.47	515	15	52.9
43.64	515	30	53.1
42.98	515	60	53.0
56.75	~60	5	53.1
57.15	~60	5	53.1
70.32	~60	5	49.5[a]
78.37	~60	5	51.5

[a] After digestion traces of selenium sulfide can still be observed.

volume of the water according to the analytical method is replaced by a solution of potassium bromide an elimination of iodine does not appear. A consumption of sodium thiosulfate standard solution cannot be observed. The concentration of the potassium bromide solution should be adjusted according to the amount of formed hydrobromic acid by the analysis. Self-evident, bromide ions are required to remove the excess of DBH. For the electrophilic substitution of 5-sulfosalicylic acid DBH has to be transferred to elemental bromine [8,11]. The former results show, that blank values in presence of hydrobromic acid are not required for the assay of selenium sulfide with DBH–HAc.

3.3. Determination of the sulfur content in selenium sulfide using DBH

Furthermore, the sulfur content of selenium sulfide can be determined with DBH–HAc. The excess of DBH is not allowed to be removed with 5-sulfosalicylic acid and converts together with selenious acid potassium iodide to iodine. On the basis of blank values the consumption of DBH for the oxidation of sulfur can be calculated. A sulfur content of 46.4% is found, which corresponds to the determined selenium content of the selenium sulfide of 53.1% Se resp. a calculated sulfur content of 46.9% (100–53.1). A standard deviation of 1.35 is obtained. The weight of selenium sulfide should be chosen in a manner, that only a small DBH excess for the oxidation is applied. DBH and arising hydrobromic acid yield elemental bromine, which can escape partially when opening the flask. Too high sulfur values are found. Thus, the border of the flask has to be moistened at first. Then the stopper of the flask is opened only a little, so that water is soaking preferably between the stopper and the grinding. The bromine vapors have to be absorbed by vigorously shaking. Apparently, at first selenious acid is not quantitatively reduced to elemental selenium by hydroiodic acid in presence of a high excess of iodine. Therefore, after a waiting period of 15 min under protection from light the meanwhile eliminated iodine is titrated again.

DBH–NaOH cannot dissolve neither selenium sulfide nor sulfur.

4. Conclusions

The simplification of the method determining selenium sulfide with DBH is evident in comparison to USP 2000 and PH. EUR. 1997. The determination can be performed at room temperature without a remarkable elimination of elemental bromine and dissolves the analyte during 5–10 min, when DBH/HAc instead of fuming nitric acid serves as oxidant. Also the sulfur content of selenium sulfide can be determined using DBH.

It must be pointed out, that this method is only checked for pure selenium sulfide corresponding to the pharmacopeias. Further investigations are necessary to verify the practicability of the method using DBH for pharmaceutical formulations such as antiseborrheic lotions, shampoos, pastes and suspensions.

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