each case were symmetrical, whereas the peaks showed some tailing on Column 1. The column selected is thermally stable at elevated temperatures and is often used at temperatures up to 75°.

Limits of detectability for the two most common synthetic estrogens, diethylstilbestrol and dienestrol, reached the nanogram level. In fact, when 1 ng of each compound was injected onto the chromatographic column, using a 20% 2-propanol-water mobile phase and a column temperature of 70°, a peak height response twice that of the noise level was observed. However, there are indications that Column 1 might prove more useful in submicrogram identification studies, since the synthetic estrogens can be eluted using a mobile phase containing a higher percentage of water, a solvent composition trend resulting in increasing photometric absorption.

Figure 5 shows an actual separation of the synthetic estrogen hormone diethylstilbestrol from two other drugs, methyltestosterone and reserpine, which are sometimes found in combination. In this particular case the methyltestosterone was present in approximately a 20-fold excess. The chromatogram shows the relative position of phenothiazine internal standard.

SUMMARY

The method proposed provides for the direct isolation of the synthetic estrogens without derivatization and appears applicable when these compounds are present in various dosage forms. Studies have indicated that compounds often present in combinations will not interfere with the method. In addition, the chromatographic patterns that result when synthetic estrogens undergo photochemical or hydrolytic change may be used for identification as an adjunct to the retention time.

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Specific Analysis for Homatropine Methylbromide in Syrups

F. F. CANTWELL ˣ, M. DOMJAN, and C. F. HISKEY

Abstract ☐ A sensitive, specific, and stability-indicating method is described for the analysis of homatropine methylbromide in complex pharmaceutical syrups. The procedure involves the isolation of methylhomatropinium ion on a cation-exchange resin column followed by on-column hydrolysis to mandelate ion by treatment with sodium hydroxide. The alkaline eluate is washed with chloroform and acidified. Ceric reagent is added to oxidize mandelic acid to benzaldehyde, which is then extracted into isooctane and measured by UV spectrophotometry. The procedure is routinely applied to complex syrups and is suitable for analyzing aged syrup samples.

Keyphrases ☐ Homatropine methylbromide—analysis in complex pharmaceutical syrups, ion-exchange separation and UV spectrophotometry ☐ Column chromatography, ion exchange—analysis of homatropine methylbromide in complex pharmaceutical syrups ☐ UV spectrophotometry—analysis, homatropine methylbromide in complex pharmaceutical syrups

The requirements of an analytical method for homatropine methylbromide (I) in pharmaceutical syrups include both sensitivity and selectivity. The drug is presently marketed in doses as low as 0.03 mg/ml and in formulations containing several other active ingredients, preservatives, buffers, flavors,

Table I—Recovery of Benzaldehyde Measured by Optical Absorbance *versus* Oxidation Time[a]

Minutes	$A_{242\ nm}$	$A_{242\ nm} - A_{263\ nm}$
5	0.926	0.887
10	0.944	0.905
15	0.952	0.909
20	0.950	0.910
25	0.952	0.909
30	0.952	0.909
35	0.952	0.909

[a] Milligrams of I per sample = 0.656, milligrams of ammonium chloride per sample = 86, and milliliters of ceric reagent = 8.0.

Table II—Recovery of Benzaldehyde Measured by Optical Absorbance as a Function of Amount of Resin and Volume of Sodium Hydroxide Eluent[a]

Resin, ml	Cation-Exchange Capacity, mEq/Column[b]	Volume of 1 *N* NaOH Eluent, ml	$A_{242\ nm}$	$A_{242\ nm} - A_{263\ nm}$
4	1.6	2 × 5	0.930	0.888
4	1.6	2 × 5 + 3	0.930	0.888
4	1.6	5 × 5	0.938	0.893
5	2.0	5 × 5	0.930	0.888
6	2.4	5 × 5	0.930	0.888
7	2.8	5 × 5	0.927	0.887
0	—	—	0.945	0.903

[a] Oxidation time = 25 min; milligrams of I per sample = 0.662, and milliliters of ceric reagent = 8.0. [b] Exchange capacity = 0.4 mEq/ml from manufacturer's label.

dyes, and sweeteners. Furthermore, if an analytical method is to be stability indicating it must be specific for homatropine methylbromide in the presence of its hydrolytic degradation products, mandelic acid and tropinium methylbromide.

Classical methods employed in the analysis of homatropine methylbromide in syrups involve the precipitation of an insoluble salt of the methylhomatropinium cation (II) by anions such as the reineckate, silicotungstate, and tetraiodomercurate, followed by colorimetry (1) or turbidimetry (2, 3). These methods lack the sensitivity, selectivity, or specificity required for syrup analysis at low doses.

The recently described colorimetric procedure involving chromogenesis with Dragendorff's reagent (4, 5) is also nonspecific and, therefore, requires separation of homatropine methylbromide from other amines present to achieve specificity. Compound I may also be analyzed by conversion to the hydroxamic acid derivative of mandelic acid, followed by colorimetric measurement of a ferric hydroxamate complex (6). This method is stability indicating for II but it lacks the sensitivity of the procedure reported in the present paper. The recently published chromatographic procedure for I in tablets and elixirs (7) has been found inapplicable to the present syrup formulations.

Chafetz (8) employed a procedure for esters of mandelic acid such as II; it involves alkaline hydrolysis followed by oxidation to benzaldehyde, extraction, and spectrophotometry. This procedure is quite satisfactory for the analysis of many simple formulations. However, the large amount of oxidizable substances present in most syrups interferes with this oxidation step and produces background absorbance in the final spectrogram. Therefore, it seemed desirable to separate II from many of these substances prior to the hydrolysis and oxidation steps.

This laboratory has been using cation exchange to separate the II-ion from various formulations, and recently a procedure was reported (9) which involves ion-exchange separation of II from syrups and other liquid formulations, followed by UV spectrophotometry of the eluted II. The method is applicable only to relatively high doses of drug.

The present paper describes a sensitive, specific, and stability-indicating method of analysis for I in syrups. The method involves separation of II from noncationic syrup components by cation exchange, followed by on-column alkaline hydrolysis and elution and removal of amine components from the resulting mandelic acid by chloroform extraction. Quantitation is achieved by ceric-ion oxidation to benzaldehyde followed by salting-out extraction into isooctane and spectrophotometric determination. A wash step is included to reduce the small background absorbance occasionally present in aged samples.

EXPERIMENTAL

Apparatus—A recording spectrophotometer[1] was used to record the spectrogram of benzaldehyde in isooctane solution. Matched 1.000-cm, fused silica, bottle-type cells were used in making all spectrophotometric measurements. The ion-exchange columns used were 0.8-cm i.d. × 19-cm long glass tubing with a Teflon stopcock at the bottom and a 2.5-cm i.d. × 10-cm reservoir at the top.

Reagents—A strongly acidic cation-exchange resin[2], 50–100 mesh, H^+ form, was used. Before use it was conditioned as described later.

Ceric ammonium sulfate[3] was reagent grade, and isooctane was 99.5+% practical grade[4]. Compound I was NF grade, and the other chemicals used were either reagent grade or spectral grade. Other drugs, preservatives, dyes, and excipients used in preparing the "blank syrup" were USP or NF grade where applicable. Otherwise, they were of standard pharmaceutical grade.

The ceric reagent was approximately 0.2 *M* ceric ammonium sulfate in 6 *N* sulfuric acid. It was prepared by suspending 31.6 g of ceric ammonium sulfate dihydrate in 250 ml of 6 *N* sulfuric acid, stirring overnight, and filtering off the undissolved solid.

Preparation of Resin Column—The specific volume of resin (4–7 ml), measured in a small graduate as the settled volume under water, was quantitatively rinsed into the glass column which had a small wad of glass wool placed in the bottom. The resin was conditioned by successively passing 6 *M* hydrochloric acid, water, and 1 *M* sodium hydroxide through it. The resin is sufficiently clean when the 1 *M* sodium hydroxide effluent shows an absorbance of less than 0.025 at 242 nm when measured in a 1-cm cell against 1 *M* sodium hydroxide as the reference.

After cleaning, the resin was rinsed successively with water, 50 ml of 6 *M* hydrochloric acid, water, 50 ml of 10% ammonia, and, finally, water until the effluent was neutral to litmus. The resin is in the ammonium form at this point and is ready for use in the assay.

General Procedure—Aqueous syrup or standard solutions containing 0.012–0.033 mg I/ml were prepared by appropriately diluting an aliquot of a syrup or a stock standard solution. The solution was filtered if not clear, and an aliquot of the clear solution containing 0.66 mg of I was pipeted into the reservoir on top of the resin column and allowed to flow through the resin at a rate

[1] Coleman-Hitachi, model EPS-3T.
[2] AG-50W-X1, Bio-Rad Laboratories.
[3] G. F. Smith Co.
[4] Eastman Organic Chemicals.

Table III—Composition of "Blank Syrup"[a]

Ingredients	Milligrams per Milliliter	Milliequivalents Cation per Milliliter
Active ingredients:		
Pyrilamine maleate	2.5	0.0124
Codeine phosphate	2.0	0.0049
Dextromethorphan hydrobromide	2.0	0.0074
Hydrocodone bitartrate	1.0	0.0020
Phenylephrine hydrochloride	2.0	0.0103
Ammonium chloride	12.0	0.224
Excipients:		
Methylparaben	13.5	—
Propylparaben	1.5	—
Sodium citrate dihydrate	4.2	0.0428
Citric acid	8.4	0.131
Sorbo	7.5% v/v	—
Liquid sugar	60.0% v/v	—
Carkole brown shade, 60%	0.015	—
FD&C Yellow No. 6, 92%	0.33	—
FD&C Red No. 2, 92%	0.109	—
Minoline green	0.050	—
FD&C Casiline Orange, 92%	0.080	—
Imitation loganberry flavor	0.35% v/v	—
Imitation cherry flavor	0.20% v/v	—
Imitation wild cherry flavor	0.04% v/v	—
Caramel	0.05%	—
Total		0.435

[a] In the experiments, a 20.0-ml aliquot of this syrup in 50 ml of solution was passed through the resin column.

of 0.4 ml/min. The reservoir was rinsed with 5–10 ml of water at the same flow rate, and then the resin bed was washed with eight 25-ml portions of water at a rate of about 2 ml/min. The final few milliliters of wash water was collected and its absorbance at 242 nm was measured to ensure that all noncationic UV absorbers had been removed. In every case the absorbance was less than 0.06 at this point.

Elution was accomplished by passing two 5-ml portions and one 15-ml portion of 1 *M* sodium hydroxide solution through the resin, again at a rate of 0.4 ml/min, allowing each portion of eluent to run completely into the resin before adding the next. This hydrolyzed the II to mandelate ion on the resin bed and eluted the latter. The alkaline eluate was collected in a 125-ml separator fitted with a Teflon stopcock and extracted with two 25-ml portions of chloroform. The chloroform layers were discarded. Filtered air was then bubbled through the aqueous solution until the odor of chloroform had completely disappeared.

Next, 8.0 ml of the ceric reagent and 25.0 ml of isooctane were added and the mixture was agitated for 25 min; then 8.0 g of sodium chloride was added and the separator was shaken for about 1 min. The phases were allowed to separate, and 20.0 ml of the clear isooctane phase (centrifuge if emulsified) was pipeted into a 50-ml ground-glass-stoppered centrifuge tube. This was extracted in the centrifuge tube with 8.0 ml of 1 *M* hydrochloric acid solution, 32% in sodium chloride. The phases were allowed to separate, and a portion of the clear isooctane layer was scanned against isooctane on a recording spectrophotometer between 340 and 220 nm.

When using the proposed procedure for the analysis of syrups, the milligrams of I per milliliter of syrup was calculated by the formula:

$$\text{mg I/ml syrup} = \frac{(A_{242\,\text{nm}} - A_{263\,\text{nm}})\ \text{sample}}{(A_{242\,\text{nm}} - A_{263\,\text{nm}})\ \text{std.}} \times \frac{\text{mg I std.}}{\text{ml syrup}} \quad \text{(Eq. 1)}$$

where "mg I std." and "ml syrup" are the amounts loaded onto the resin column.

Procedure without Ion Exchange—In some experiments the ion-exchange step was eliminated. In these experiments, 25.00 ml of an aqueous solution that was 1 *M* in sodium hydroxide and contained about 0.66 g of I and 0–500 mg of ammonium chloride, as specified below, was pipeted into a 125-ml separator. After allowing it to stand for at least 30 min to ensure complete hydrolysis, the solution was extracted with two 25-ml portions of chloroform and the aqueous phase was bubbled free of the odor of chloroform as already described. Then a volume of from 6.0 to 10.0 ml of the ceric reagent was added, as specified below, along with 25.0 ml of isooctane, and the mixture was agitated for the specified time. From this point the remainder of the procedure is identical to that given under *General Procedure*.

RESULTS AND DISCUSSION

This section reports the results of experiments designed to determine the optimum conditions for analysis such as oxidation time, reagent concentrations, and elution conditions. It also includes the results of analyses performed on a synthetic syrup formulation, the results obtained when standard additions were made to commercial syrups, and typical results of analyses of commercial syrups.

Optimum Conditions of Analysis—To optimize the post-ion-exchange steps in the procedure, the influence of oxidation conditions was investigated in a simulated column eluate solution. Patel and Lemberger (10) reported a second-order rate constant of 1.11 liters $\text{mole}^{-1}\ \text{sec}^{-1}$ for the alkaline hydrolysis of I at 20°. Thus, the (pseudo) first-order half-time in 1 *M* sodium hydroxide is 0.62 sec. It is apparent that the minimum 30-min hydrolysis time in approximately 1 *M* sodium hydroxide, called for in the *Procedure without Ion Exchange* in the present study, is more than adequate for quantitative hydrolysis of I.

To determine the effect of oxidation time on the final benzaldehyde recovery, an experiment was performed in which the amounts of I, ammonium chloride, sodium hydroxide, and ceric oxidant were held constant while the time of oxidation was varied. Ammonium chloride was included because the resin column is used in the ammonium form and, consequently, there is ammonia in the column eluate solution in which the oxidation is performed. The amount of ammonium chloride included in this experiment is equivalent to the amount of ammonia present on 4 ml of resin. Under the experimental conditions, maximum recovery of benzaldehyde is obtained for oxidation times of 15–35 min (Table I).

The third column in Table I gives the difference between the absorbance at the benzaldehyde maximum and minimum. This figure was used for calculating assay results since it is less sensitive to background absorbance than the absorbance at the maximum alone.

To determine the effect of using different amounts of ceric reagent and the influence of ammonium chloride on the quantitation, an experiment was performed in which these quantities were varied while other conditions were held constant as described in the *Experimental* section. It was found that variation of the volume of ceric reagent from 6.0 to 10.0 ml changed the final absorbance by less than 1.5% and that variation of the amount of ammonium chloride from 0 to 500 mg in the 25.00-ml sample had no effect on the final absorbance.

The distribution coefficient of benzaldehyde between isooctane and water is about 9 and that between isooctane and 32% aqueous sodium chloride[5] is about 45. Consequently, the addition of sodium chloride is made to the separator after oxidation is complete to improve the extraction of benzaldehyde. Addition of the salt prior to complete oxidation is undesirable because it would alter the oxidation potential of the Ce (IV)–Ce (III) half-reaction (11) and prolong the oxidation step. Washing of the isooctane layer to reduce the background absorbance was done with 32% sodium chloride in dilute hydrochloric acid for the same reason. The net loss of benzaldehyde due to incomplete extraction in the oxidation and wash steps is thus expected to be about 3%.

The absolute recovery of benzaldehyde in the oxidation step may be calculated by comparing the $A_{242\,\text{nm}}$ with that predicted from a knowledge of the molar absorptivity of benzaldehyde [$\epsilon_{242\,\text{nm}}$ = 14,000 (12)] and the amount of I taken. The recovery obtained for standards not subjected to ion exchange, using 8.0 ml of ceric reagent and 25 min oxidation time, was 95%. This figure, plus the calculated loss of 3% due to incomplete extraction, yields a total absolute recovery of about 98% of the theoretical amount. This recovery is equal to 100% within the experimental

[5] Determined by T. Meites in this laboratory.

Table IV—Analysis of Simulated Syrups by the Proposed Method[a]

Blank Syrup	Syrup Passed through Resin[b], ml	I Added, mg	Mandelic Acid Added, mg	$A_{242\ nm}$	$A_{242\ nm} - A_{263\ nm}$
Room temperature sample	20.0	0.680	0	0.943, 0.933	0.898, 0.890
	20.0	0	0	0.008	0.005
	20.0	0	0.270	0.012	0.003
60° sample	20.0	0.680	0	0.987, 0.985	0.906, 0.900
	20.0	0	0	0.062	0.023
No syrup (standard), subjected to ion exchange	0	0.680	0	0.958, 0.957	0.914, 0.913

[a] Used 4.0-ml resin column; oxidation time = 25 min, milliliters of ceric reagent = 8.0. [b] The 20.0 ml syrup contained in 50.0 ml of solution passed through the resin.

Table V—Analysis of Commercial Syrups for I[a]

Syrup Sample	Label Claim, mg I/ml	Age of Syrups, years	Added I, mg/ml	Milligrams I per Milliliter Found[b]	Recovery of Added I, %
A	0.033	7.0	0.0	0.0335	—
A	0.033	7.0	0.0342	0.0680	101
B	0.055	0.5	0.0	0.056	—
C	0.11	1.0	0.0	0.108	—
D	0.165	0.2	0.0	0.170	—
E	0.33	0.7	0.0	0.342	—
F	0.33	7.1	0.0	0.274	—
F	0.33	7.1	0.342	0.614	99

[a] Oxidation time = 25 min, milliliters of resin = 4.0, and milliliters of ceric reagent = 8.0. [b] Calculated by the formula:

$$\frac{(A_{242nm} - A_{263nm})\ \text{sample}}{(A_{242nm} - A_{263nm})\ \text{std. on resin}} \times \frac{\text{mg I std. on resin}}{\text{ml syrup on resin}}$$

error of the molar absorptivity used, indicating that the oxidation of mandelate to benzaldehyde is virtually quantitative.

Conditions of Ion-Exchange Separation—The strongly acidic sulfonate resin column was used in the ammonium form rather than in the hydrogen form because it was felt, initially, that acid hydrolysis of II on the resin column would be less likely. No experiments have been done to verify this, and it is quite possible that the H^+ resin could be used in the procedure. Compound II is, in fact, rather stable toward acid hydrolysis (8).

An experiment was performed to evaluate the influence of various parameters on the ion-exchange separation of II. A constant amount of I was loaded onto columns containing various amounts of resin, washed with 200 ml of water, and eluted with different volumes of 1 *M* sodium hydroxide into 125-ml separators. Then an amount of 1 *M* sodium hydroxide was added to the separator to bring the total volume of solution to 25 ml. The analysis was performed from this point on as already described.

It is apparent from Table II that the 4.0 ml of resin and the 2 × 5 + 15 ml of sodium hydroxide eluent called for in the *General Procedure* are quite adequate to retain I quantitatively, to hydrolyze II, and to elute mandelate. The last row in Table II shows the absorbance found for a sample containing the same amount of I in 25 ml of 1 *M* sodium hydroxide but not subjected to ion exchange prior to oxidation. It can be seen from Table II that all of the ion-exchange conditions used afforded the same recovery, *i.e.*, 98–99%, compared to the standard that was not subjected to ion exchange. This slight loss of I in standards subjected to ion exchange has been found to vary between 0.5 and 2.0% through numerous analyses. This apparent loss of I in the ion-exchange step is small and reproducible within the experimental error. To eliminate any systematic bias as a result of it, the standards called for in the *General Procedure* are subjected to the ion-exchange step as are the samples.

Analysis of Simulated Syrup—To verify the quantitative character of the proposed analytical procedure, a "blank syrup" was prepared in the laboratory. It contained many common drugs, preservatives, flavors, dyes, and other excipients but no homatropine methylbromide (Table III). A portion of the syrup was stored at room temperature for about 2 weeks, and another portion was stored at 60° for the same period. Then 40.0-ml aliquots of each were pipeted into 100-ml volumetric flasks, an aliquot of an aqueous stock solution containing 1.360 mg of I was added to each, and the solutions were diluted to 100 ml with water. Then 50.0-ml aliquots were analyzed by the *General Procedure* for I. The experiment was repeated on the room temperature and 60° samples without the addition of I and also on the room temperature sample without I but with the addition of an amount of mandelic acid equivalent to 0.66 mg of I.

These last three blank samples were run to determine the background spectrum and to demonstrate that mandelic acid is not retained on the resin column under the conditions of analysis. The amount of sample taken was equal to that which would be used for a syrup containing about 0.033 mg I/ml; furthermore, the number of ingredients is considerably greater than would be found in any one pharmaceutical formulation. The third column of Table III lists the number of milliequivalents of exchangeable cationic substances in a milliliter of the prepared syrup. Since the 50.0 ml of diluted syrup solution that is passed through the resin in the loading step contains 20.0 ml of syrup, the total of exchangeable cations passed through the resin in this experiment is 8.7 mEq.

Although this figure considerably exceeds the total exchange capacity of the 4-ml resin bed, 98–99% recovery of I was obtained in the analyses of both room temperature and 60° samples when compared to the standard subjected to ion exchange (Table IV). In addition, the background absorption is small, even in the 60° sample, and is roughly constant between 263 nm, the wavelength of minimum absorbance, and 242 nm, the wavelength of maximum absorbance of benzaldehyde. Thus, by subtracting the former absorbance from the latter in all samples and standards, an adequate background correction can be made even in the analysis of samples that are several years old or that have been stored at elevated temperatures.

The blank sample containing mandelic acid, the hydrolysis

product of I, yielded no absorbance at 242 nm, indicating that the method is stability indicating with respect to hydrolytic decomposition of I.

Analysis of Commercial Syrups—Typical analyses of six commercial syrups, 0-7 years old, are presented in Table V. These syrups contained from one to three of the active ingredients listed in Table III at levels equal to or less than those listed, plus liquid sugar and various of the dyes, flavors, preservatives, and excipients listed. To verify that the conditions that prevail in old syrups do not interfere with the analysis, the standard addition technique was employed with Syrups A and F. In this technique, one aliquot of the syrup was analyzed in the regular manner while a second, equal aliquot was analyzed after the addition of an amount of I equal to that in the syrup itself. The resulting isooctane solution for this sample was diluted in half prior to scanning on the spectrophotometer. It can be seen from Table V that the recovery of added standard is quantitative.

When analyzing aged samples, emulsion formation is often encountered in the oxidation step. However, a clear isooctane layer is readily obtained in these cases upon centrifugation. In addition, old samples of syrup produce considerable darkening of the ion-exchange resin and a small amount of background in the benzaldehyde spectrum, even after washing with the hydrochloric acid-salt solution. This background is readily corrected for by using the absorbance difference between 242 and 263 nm in calculations.

Although phenylephrine is known to undergo periodate oxidation to *m*-hydroxybenzaldehyde (13), no spectral evidence of this strong UV absorber was detected in the final isooctane solution resulting from the analysis of commercial syrup or blank syrups containing phenylephrine.

SUMMARY

The proposed method of analysis for homatropine methylbromide in syrup formulations is sensitive, specific, and stability indicating. It permits the routine, accurate analysis of I in syrups at the lowest dosage levels commercially available and is suitable for the analysis of darkened, aged samples.

No attempt was made to determine the maximum sensitivity of this method. It is apparent, however, that lower doses and different formulations, containing larger amounts of other substances, could be analyzed for I by this method or by a modification of it using, for example, a larger amount of ion-exchange resin and a longer path length cell for recording the spectrogram.

The method and minor modifications of it have been used routinely for several years for the analysis of I in syrups, elixirs, and complex tablet formulations.

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Determination of Sodium Penicillin G in Disodium Carbenicillin Preparations

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Abstract ☐ Aqueous solutions of disodium carbenicillin containing sodium penicillin G (sodium benzylpenicillin) are chromatographed by TLC using silica gel on aluminum foil and acetone-chloroform-acetic acid-water (50:45:5:1 v/v) as a developing solvent. The location of penicillin G is determined by reference to standard strips cut from the edges of the chromatogram and visualized colorimetrically. The appropriate area is removed and penicillin is eluted from the silica with phosphate buffer at pH 7.0. The amount of penicillin is determined spectrophotometrically after formation of penicillenic mercuric mercaptide formed by heating penicillin with an imidazole reagent containing mercury.

Keyphrases ☐ Carbenicillin—TLC analysis of penicillin G (benzylpenicillin) content ☐ Disodium carbenicillin—TLC analysis of sodium penicillin G (sodium benzylpenicillin) content ☐ Penicillin G (sodium)—TLC analysis as impurity in disodium carbenicillin ☐ Sodium penicillin G—TLC analysis as impurity in disodium carbenicillin ☐ Benzylpenicillin—TLC analysis as impurity in carbenicillin ☐ TLC—analysis, sodium penicillin G (sodium benzylpenicillin) in disodium carbenicillin

Disodium carbenicillin (the disodium salt of α-carboxybenzylpenicillanic acid) is a semisynthetic penicillin prepared from monobenzylphenylmalonyl chloride and 6-aminopenicillanic acid. A subsequent reduction of this compound under specific conditions yields disodium carbenicillin.