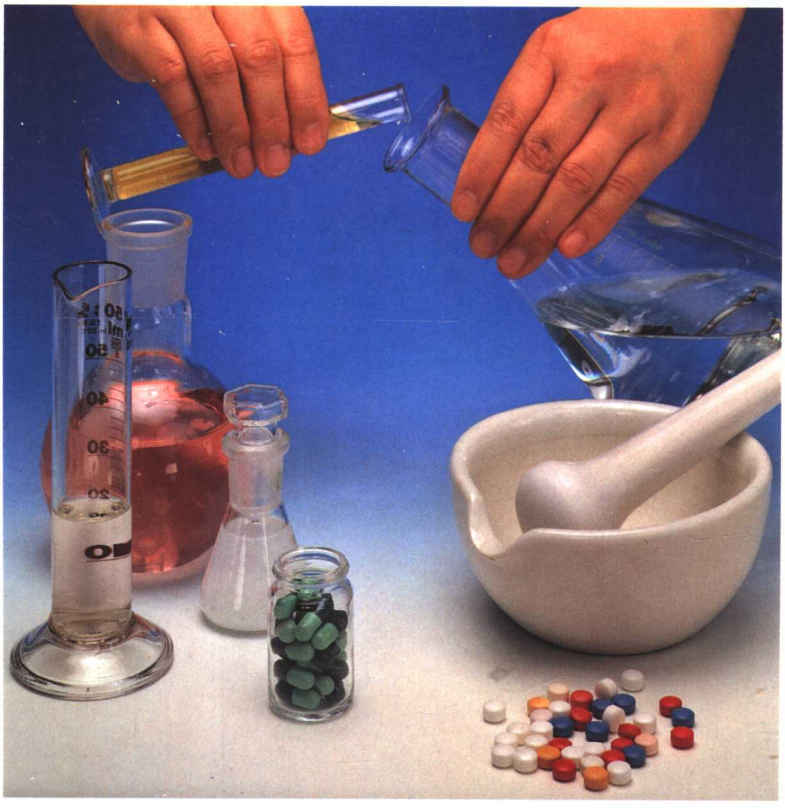
BASIC TESTS FOR DRUGS

Pharmaceutical substances, medicinal plant materials and dosage forms



World Health Organization
Geneva

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World Health Organization
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1998

WHO Library Cataloguing in Publication Data

Basic tests for drugs:pharmaceutical substances, medicinal plant materials and dosage forms.

1.Pharmaceutical preparations—Chemistry 2.Plants, Medicinal—chemistry 3.Dosage forms—chemistry 4.Indicators and reagents 5.Chemistry, Analytical—handbooks 6.Quality control—methods 7.Manuals

ISBN 92 4 154513 5 (NLM Classification: QV 39)

Designed by WHO Graphics
Typeset in Hong Kong
Printed in England

97/11753—Best-set/Clays—8000

Contents

1. Introduction

This manual has been designed to be used in conjunction with two earlier World Health Organization (WHO) publications, *Basic tests for pharmaceutical substances*[1] and *Basic tests for pharmaceutical dosage forms*.[2] Most of the pharmaceutical substances and dosage forms covered are included in the WHO Model List of Essential Drugs.[3] The present volume describes procedures for testing a further 23 pharmaceutical substances and 58 pharmaceutical dosage forms and also for testing four medicinal plant materials (sections 3–5).

These basic tests represent one of the many elements of quality assurance in the pharmaceutical supply system. They have been devised with the following objectives:

(a) to provide a simple and readily applicable method for verifying the identity of a substance, using a limited range of easily available reagents, when the labelling and physical attributes give rise to doubt;

(b) to provide a practicable means of confirming the identity of a substance when a fully equipped laboratory is not available;

(c) to indicate whether gross degradation has occurred in certain substances that are known to decompose readily under adverse conditions.

Basic tests are not, in any circumstances, intended to replace the requirements of *The International Pharmacopoeia*[4] or other pharmacopoeial monographs. These give an assurance of quality whereas basic tests merely confirm identity.

In 1994, the WHO Expert Committee on Specifications for Pharmaceutical Preparations[5] agreed that the scope of these tests should be extended to include additional information and references to other simple test methodologies.

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[1] *Basic tests for pharmaceutical substances*. Geneva, World Health Organization, 1986.

[2] *Basic tests for pharmaceutical dosage forms*. Geneva, World Health Organization, 1991.

[3] *The use of essential drugs. Seventh report of the WHO Expert Committee*. Geneva, World Health Organization, 1997 (WHO Technical Report Series, No. 867).

[4] *The International Pharmacopoeia*, 3rd ed. Geneva, World Health Organization. Volume 1: *General methods of analysis*, 1979. Volume 2: *Quality specifications*, 1981. Volume 3: *Quality specifications*, 1988. Volume 4: *Tests, methods, and general requirements. Quality specifications for pharmaceutical substances, excipients, and dosage forms*, 1994.

[5] *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-fourth Report*. Geneva, World Health Organization, 1996 (WHO Technical Report Series, No. 863).

The usefulness of simplified analytical technology and supporting elements, such as thin-layer chromatography (TLC) kits, reference tablets and associated training materials, was fully endorsed by the Committee. They are considered to be valuable tools for primary screening and could play an important part in identifying counterfeit and spurious products. Several collections of simplified tests are therefore reviewed in this manual (see section 2).

Degradation during storage and transportation is of particular importance in tropical countries. Indeed, an expiry date determined for a temperate climate may be inappropriate in a tropical region even when high standards of packaging are met. For this reason, particular importance is accorded to visual inspection of dosage forms, since this frequently provides a first vital indication of degradation. This also applies in cases where there are reasons to suspect quality defects due to poor manufacture, tampering, or counterfeiting. Visual inspection should precede any testing. Inspection procedures are outlined in *Basic tests for pharmaceutical dosage forms.*

Basic tests need not be carried out by fully qualified pharmacists or chemists, but they should be performed by persons with some understanding of analytical chemistry such as that acquired in courses for pharmaceutical assistants.

The facilities needed for carrying out basic tests, the equipment required and methods for the determination of melting characteristics are described in detail in the two earlier manuals of basic tests. Reagents additional to the ones described in those two manuals are listed in section 6.

Several tests are described for most preparations. Not all of these need to be applied to any one sample. If, however, there is any reason to suspect that the product is mislabelled or substandard, all tests described should be performed. By their nature, simplified tests cannot be totally reliable. An adverse result, even in one test, should be taken as a warning of potential unsuitability of a drug. In these circumstances, a final conclusion should not be drawn until a full analytical examination has been carried out in a properly equipped quality control laboratory.

For easy reference, section 7 provides a cumulative index of WHO basic tests.

Comments on the tests described are invited and should be addressed to: Quality Assurance, Division of Drug Management and Policies, World Health Organization, 1211 Geneva 27, Switzerland.

2. Other collections of simple tests

Various collections of simple tests other than the basic tests published by WHO are available for verifying the identity of drugs, and a selection of these are reviewed here.

In addition to their use in identification, many of these tests can be used to estimate the content of active ingredients; however, they employ more sophisticated techniques than are required for the WHO basic tests, including volumetric or spectrophotometric analysis and thin-layer chromatography. Some of these methods also require reference materials and additional equipment and reagents, as well as better training for operators.

As with the basic tests, these simple tests are not intended to replace pharmacopoeial analyses. Before any of these collections of tests are used, their suitability should be evaluated, and users should validate the methods.

Thin-layer chromatography

Primary screening of imported pharmaceutical substances and dosage forms is designed to establish that consignments contain the right drug(s) in the right amount(s). National ports of entry for such consignments may lack access to standard laboratory resources, but it is important that this primary screening can be done quickly, with simple equipment, at low cost, and without the need for highly trained personnel. TLC techniques have been found to be suitable for the purpose. Both the initial capital investment and the operating costs are low, a large number of samples can be handled in a relatively short time, and results are reliable.

A primary screening facility, with the capacity to conduct both TLC and WHO basic tests and examine product labelling, requires a minimum of two trained individuals. Technical, rather than professional, training is generally necessary, and manual dexterity and literacy are minimum requirements. The test area should be protected but control of temperature and humidity is not essential.

The interested reader can find further discussion of analytical screening procedures in *WHO drug information*, 1997, 11(3):128–130 (Layloff TP, The importance of analytical procedures in regulatory control).

Thin-layer chromatography tests developed by the World Health Organization (unpublished)

More than 150 TLC procedures were developed in the early 1980s through collaborative research conducted under the auspices of WHO, including 128 tests for pharmaceutical substances and 29 for formulations. The majority of these procedures were for drugs contained in the WHO Model List of Essential Drugs. These tests were never published since it was felt that further research is required to reduce the number of mobile phase systems employed (currently over 40). The project has not been finalized but further studies to re-evaluate some of these tests are proposed.

Thin-layer chromatography tests developed in the USA (language: English)

Standardized TLC procedures were developed by a team of researchers from the Division of Drug Analysis of the United States Food and Drug Administration (*1*) in the early 1990s. The test methods are based on the use of a portable kit, which features plastic bags for development and staining (detection) and contains other accessories required to perform the tests. Training materials are included to facilitate the practical application of the test kits. All the tests were field-tested in a number of countries.

The application of the tests is described in detail. These methods are suitable for rapid screening of drugs at ports of entry, pharmacies, or distribution centres, or in areas lacking resources for other methods of analysis. If any results indicate that products do not comply with the specification, the tests should be repeated. Suspect samples must be submitted for official analysis by legal reference methods (LRM).

Test procedures are described for 69 products, 38 of which are on the WHO Model List of Essential Drugs. Small plastic plates (5 × 10 cm) coated with silica gel are recommended. Mobile phase systems are prepared from a list of eight solvents. Sample solutions are prepared with one or two of the solvents used for the mobile phase systems. (*Note*: chloroform and other toxic halogen compounds are not recommended for use.) The two detection methods applied are the exposure to iodine vapour and ninhydrin methods.

Analyses are of a semi-quantitative nature. The test sample is prepared from one unit dose of the product under examination, thus avoiding the influence on the tests of operations such as sample weighing and the preparation of sample solutions from composite samples of dosage units. For detection purposes, a spot of the test solution is compared with two reference spots representing the upper and lower limit concentrations: 85% and 115% (120% as the upper limit for certain antibiotics) in accordance with compendial limits for unit dose uniformity. A single analysis is therefore sufficient to confirm (or disprove) the identity of the active ingredient and to estimate the assay value and the unit dose uniformity of the product.

Reference materials are needed for all the tests in this collection. Either primary (Chemical Reference Substances, CRS) or secondary standards may

be used. Secondary standards can be obtained from previously analysed samples or from reputable suppliers of drug substances.

Since analytical or semi-micro-balances are required for the weighing of reference standards, a study is in preparation to develop reference tablets, i.e. standards in the form of accurately weighed units in tablet form.

The advantage of these tests is that identity, assay value and unit dose uniformity can be determined in one operation. Furthermore, testing is focused on a single method and requires a minimum of equipment. The test kits provided contain basic solvents and reagents and are suitable for analysis outside the laboratory.

Simple thin-layer chromatography tests developed in Germany
(languages: English, German)

The German drug industry (through the German Pharma Health Fund) supported work by the Pharmaceutical Institute of the Rheinische Friedrich Wilhelms University of Bonn during the period 1988–1994 to develop a series of TLC tests for the estimation of quality of some widely used pharmaceutical products in tablet and capsule form (*2*). WHO was involved in the initial phase to develop the objectives and the scope of recommendations. The project was expanded to include testing of different brands of dosage forms from the market. The proposed methods use various types of plates and mobile phase systems, the latter employing 10 different solvents, avoiding halogenated ones, but including water. The test collection includes the results of this comparative testing and high-quality colour reproductions of the chromatograms.

Tests are published for 20 substances, most of which are on the WHO Model List of Essential Drugs. Most tests provide some means of detecting certain impurities that arise during the manufacturing process or by degradation. These studies were performed using commercial batches. For three substances there are two tests available, one of which uses a different development system, chosen specifically to detect impurities.

Tests are based on the use of precoated (mostly silica gel, occasionally cellulose) plates on glass (alternatively aluminium foil) supports, in most cases with chamber saturation. In addition to normal size plates (10 × 20 cm) small high-performance thin-layer chromatography (HPTLC) plates (5 × 5 cm) are also used. Small plates are developed in a horizontal position (Desaga–H chamber). It is recommended that the test solutions are placed as a band (3 × 15 mm), rather than a spot, to facilitate reading of the chromatograms. A shortened distance of development (7–8 cm) is recommended using normal plates to speed the test process (e.g. 10–15 minutes instead of 30–45 minutes). The distance for the development on small plates is 4 cm, which is associated with a development time of 4–5 minutes (even less than for normal plates).

The publication gives valuable advice regarding the use of reference materials for impurities. For epi- and anhydro- forms of tetracycline, for example, use

of the parent substance, decomposed in the laboratory by heating with acids, is recommended in preference to use of a CRS.

The advantage of these tests is the efficient conditions used for the identification of active ingredients of some solid oral dosage forms. In most cases these methods also allow the detection of impurities occurring during manufacture and degradation. Reliable results are achieved with shorter development times, often using greatly reduced amounts of solvents (HPTLC technique); this is more economical and offers greater safety to the operator, as well as being less damaging to the environment.

Thin-layer chromatography tests developed in Japan
(languages: English, Japanese)

At the request of the Japanese Ministry of Health and Welfare, the Committee for Countermeasures against Counterfeit and Substandard Drugs has developed TLC test procedures (*3*). Two investigations on counterfeit and substandard drugs were carried out by the Japan International Corporation of Welfare Services in 1993 and 1994. These investigations were also performed in facilities of local drug quality control laboratories in five southeast Asian countries. The development of the test collection is the result of these investigations. The Japanese Pharmacopoeia Society also collaborated on this project during 1993–1994. Using products from the market, proposed test methods for various dosage forms were validated in quality-control laboratories by more than 30 leading Japanese pharmaceutical manufacturers.

Currently, tests are available for 29 drugs, almost all of which are included in the WHO Model List of Essential Drugs (17 are antibiotics). The drugs were selected on the basis of their association with counterfeiting. They are classified into five categories (three for antibiotics, one for analgesics and one for water-soluble vitamins). Procedures are provided for the preparation of sample solutions according to their dosage forms and for the spotting, development, detection and evaluation of chromatograms. Useful indications and notes are given concerning the preparation of TLC plates in the laboratory and the performance of the tests for a total of 45 items. For each category of drugs there are three to five mobile phase systems (18 systems in total) and two to five detection methods. For each category and each development system the retention factor R_f (the ratio of the distance travelled by the analyte to that travelled by the solvent) is given, and for each detection method a brief indication is provided regarding the expected spots, in terms of "strong", "weak", "tailing" or "no spot".

These tests are primarily designed to verify the identity of active ingredients in drugs. A rough estimate of the content of the active ingredients in the test sample can also be obtained from a comparison of the size and the intensity of the spots for test and reference samples. The collection of tests is supported by colour reproductions of chromatograms using different detection methods.

Standard equipment for TLC is needed for these tests. The tests are performed on normal size glass plates (5 × 20 cm or 20 × 20 cm) coated with silica gel either prepared in the laboratory or available commercially. Brief mention is made of the optional use of small plates (2 × 5 cm) of plastic or aluminium foil coated with silica gel. All procedures require reference materials, such as secondary standards or good quality bulk substances.

Usually there is no need to use all the listed mobile systems and detection methods to test any one drug. For verification of the identity of the active ingredient, it is satisfactory to use one appropriate mobile phase and detection method. Reliability is increased by using all the recommended mobile phase systems for each substance. When reference materials are not available it is recommended that judgement of the identity of the sample under examination is based on a comparison of the R_f values obtained, using all the mobile phase systems listed (R_f values are given in the text).

Identification and assay tests developed in France
(languages: English, French)

The National Association of the French Pharmaceutical Industry (*Syndicat National de l'Industrie Pharmaceutique*) prepared, during the period 1987–1991, a collection of test sheets for identification and assay of finished pharmaceutical products (*4*). Test methods are described on laminated cardboard sheets designed to be resistant to reagents and solvents in a laboratory setting. The field of application of these tests is not defined by the authors, but it appears that they are intended for use in the training of personnel in developing countries rather than for routine quality control operations.

Altogether there are 216 sheets, of which 111 are for preparations included in the WHO Model List of Essential Drugs. A typical sheet contains:

- three (occasionally four or five) colour/precipitation reactions for identification
- one assay method, generally based on a volumetric determination (typically, non-aqueous titration); occasionally, the endpoint is determined potentiometrically.

No limits of acceptance/rejection are indicated for the assay values.

A TLC procedure is included in 45 sheets, determination of melting point (usually of a derivative) in nine, and a spectrophotometric measurement in the ultraviolet (UV) or visible part of the spectrum as identity tests in three. In 56 sheets, two alternative assay methods are provided, one non-instrumental and the other based on the measurement of the absorbance with a UV/visible spectrophotometer.

For some 100 sheets, reference materials are required for spectrophotometric or TLC tests. It is understood that commercial substances of good (pharmacopoeial) quality may be used for this purpose.

The resources needed include:

— glassware

— melting-point apparatus

— analytical balance and an assembly for volumetric assays

— materials for TLC (for spotting, development, visualization, etc.)

— UV/visible spectrophotometer

— potentiometer

— reagents

— reference materials.

These tests provide a considerable degree of flexibility, making them suitable for use in verifying identity and estimating the content of the active ingredient of some 200 widely used products, using limited instrumentation.

Quality control methods for developing countries developed in France (language: French)

During the period 1988–1993, the Faculty of Pharmacy in Nantes (France), which is the WHO Collaborating Centre for Stability Studies of Drugs, elaborated a collection of test methods for use in developing countries (*5*). Originally, research was focused on stability testing of dosage forms to permit the measurement of the content of (unchanged) active ingredients. Later, identification procedures were added. The tests are proposed for use by quality control laboratories in developing countries which are not yet fully equipped for pharmacopoeial analyses. All the tests were developed and validated on finished products manufactured in France. They were also used in the course of stability studies on some 200 products also of French origin. In addition, the tests were all verified in the field.

Test methods for 121 formulations, 65 of which are on the WHO Model List of Essential Drugs, are available. In many cases, the same tests can be used for the corresponding drug substances. All the test sheets in this collection contain an assay procedure that measures absorbance in the UV region of the spectrum or have a volumetric titration (usually non-aqueous) and a TLC method for identification purposes. Reference materials are needed for the spectrophotometric and TLC tests.

The collection includes a general text on major analytical methods, lists of equipment and reagents required and a cost estimate for the reagents needed if only one test is performed or for all the tests described.

The simple assay methods offered can be used, *inter alia*, to monitor the stability of a number of widely used finished pharmaceutical products in the distribution system (by measuring the content of the active ingredient).

Sheets for the identification of medicines in pharmacies developed in Belgium (language: French)

During the period 1987–1993, a subcommittee of the Belgian Pharmacopoeia Committee prepared simple unofficial procedures to assist pharmacists to verify the identity of drugs supplied in pharmacies (*6*).

There are 159 test sheets, all of them for pharmaceutical substances, 17 of which are included in the WHO Model List of Essential Drugs. Typically, a sheet contains a description of the substance, information on its solubility, a melting point, and two to three colour reactions. In 36 sheets, one identity test is replaced by a TLC procedure, which refers to the general recommendations given in the Belgian Pharmacopoeia. The reference materials needed in these tests are issued by the Belgian Pharmacopoeia.

A number of the TLC procedures have a built-in "system suitability test". A test is considered invalid if it fails to reveal a secondary spot in a reference solution that contains an added impurity (e.g. another drug substance, chemically related to the test substance). This feature is considered to give these tests a certain advantage over other TLC tests.

References

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2. Pachaly P et al. *Simple thin-layer chromatographic identification of active ingredients in essential drugs*. Bonn, Pharmaceutical Institute of the Rheinische Friedrich Wilhelms University, 1994.

3. *Technology transfer promotion project for pharmaceutical field*. Tokyo, Committee on Countermeasures against Counterfeit and Substandard Drugs, 1993–1995.

4. Fabiani P, Pesez M. *Fiches d'identification et de dosage des médicaments.* [*Drugs identification and assay sheets.*] Paris, Syndicat de l'Industrie Pharmaceutique, 1987–1991.

5. Vincent-Ballereau F et al. *Contrôle de qualité des médicaments essentiels dans les pays en développement, méthodes standardisées.* [*Quality control of essential drugs in developing countries.*] Nantes, Groupe d'Etudes Epidémiologiques et Prophylactiques et Centre Collaborateur de l'OMS pour l'Etude de la Stabilité des Médicaments, Faculté de Pharmacie, 1993.

6. *Fiches de vérifications d'identité des médicaments en officine.* [*Sheets for the verification of the identity of medicines in pharmacies.*] Brussels, Secrétariat de la Commission Belge de la Pharmacopée, 1987–1993.

3. Test procedures for pharmaceutical substances

AMIKACIN SULFATE

Identity tests

Description. A white to yellowish white, crystalline powder; almost odourless.

Colour and other reactions

1. Dissolve 10 mg in 1 ml of water, add 1 ml of sodium hydroxide (~80 g/l) TS and mix, then add 2 ml of cobalt(II) nitrate (10 g/l) TS; a violet colour is produced.
2. Dissolve 0.05 g in 3 ml of water and add slowly 4 ml of anthrone TS; a bluish violet colour is produced.
3. Dissolve 20 mg in 1 ml of water and add 1 ml of barium chloride (50 g/l) TS; a white precipitate is produced which is practically insoluble in hydrochloric acid (~250 g/l) TS.

BACITRACIN ZINC

Composition. Bacitracin zinc is a zinc complex of bacitracins, polypeptides produced by the growth of an organism of the licheniformis group of *Bacillus subtilis*. The main components are the bacitracins A, B1 and B2.

Identity tests

Description. A white or pale brownish yellow powder; odourless or with a faint, characteristic odour; hygroscopic.

Colour and other reactions

1. Shake 5 mg with 1 ml of water, add 1 ml of triketohydrindene/butanol TS and 0.5 ml of pyridine R and heat to 100 °C for 5 minutes; a violet colour is produced.
2. Transfer about 0.5 g to a silica crucible and ignite. Dissolve the residue in 5 ml of sulfuric acid (~5 g/l) TS and filter. Divide the filtrate into 2 equal volumes.

(*a*) To 1 volume add 1 ml of potassium ferrocyanide (45 g/l) TS; a white precipitate is produced which is insoluble in hydrochloric acid (~250 g/l) TS.

(*b*) To 1 volume add 1 drop of copper(II) sulfate (1 g/l) TS and 1 ml of ammonium mercurithiocyanate TS; a violet precipitate is produced.

Degradation tests

Discoloration of the test substance and non-compliance with the following test usually indicate gross degradation:

Dissolve 0.10 g in 100 ml of water; a clear, colourless or slightly yellowish solution is produced.

CAPTOPRIL

Identity tests

Description. A white or almost white, crystalline powder; odour, characteristic but faint.

Colour and other reactions

1. Dissolve 10 mg in 2 ml of hydrochloric acid (0.1 mol/l) VS and add about 1 ml of iodine TS; the colour of the iodine disappears immediately and a white, turbid solution is produced.
2. Dissolve 10 mg in 2 ml of water and add 0.5 ml of lead acetate (80 g/l) TS; a white precipitate is produced.
3. Dissolve 10 mg in 5 ml of ethanol (~750 g/l) TS, add 0.5 ml of tetramethylammonium hydroxide/ethanol TS and shake. Then add 0.5 ml of triphenyltetrazolium chloride/ethanol TS and shake again; a red colour is produced.

CHLORAMPHENICOL SODIUM SUCCINATE

Identity tests

Description. A white or almost white powder; hygroscopic.

Colour and other reactions

Dissolve about 1.4 g in 5 ml of water and use as the test solution for the following tests:

1. To 1 drop of the test solution add 5 ml of ethanol (~750 g/l) TS, 0.2 g of zinc R powder and 1 ml of sulfuric acid (~100 g/l) TS and allow to stand for 10 minutes. Filter; to the filtrate add 0.5 ml of sodium nitrite (10 g/l)

TS and allow to stand for 2 minutes. Then add about 1 g of urea R and a solution containing 10 mg of 2-naphthol R in 2 ml of sodium hydroxide (~80 g/l) TS; a red colour is produced.

2. Repeat test 1 omitting the zinc R powder; no red colour is produced.
3. Carefully heat 1 drop of the test solution with 10 mg of resorcinol R and 3 drops of sulfuric acid (~1760 g/l) TS, cool and add 2 ml of water. Cool again and pour the solution into a mixture of 100 ml of water and about 1 ml of sodium hydroxide (~400 g/l) TS; a yellow-green fluorescence appears which disappears on the addition of 1 ml of hydrochloric acid (~250 g/l) TS.
4. Introduce the test solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.

Degradation tests

Discoloration of the test substance and non-compliance with the following test usually indicate gross degradation:

Dissolve 0.2 g in 10 ml of water; a clear solution is produced.

CISPLATIN

Identity tests

Description. White to yellowish crystals or a yellow powder.

***Note.* This substance is very toxic and should be handled with care.**

Colour and other reactions

1. Dissolve 5 mg in 5 ml of hydrochloric acid (~420 g/l) TS and heat to boiling. To half of the solution (keep the unused portion for test 2) add a few crystals of potassium iodide R; a brownish yellow colour is produced which changes to reddish brown on standing.
2. To the remaining solution from test 1 add a few crystals of tin(II) chloride R; a reddish orange colour is produced which changes to reddish brown on standing.
3. Transfer 0.05 g to a glass dish and add 2 ml of sodium hydroxide (~80 g/l) TS. Evaporate to dryness and dissolve the residue in a mixture of 0.5 ml of nitric acid (~1000 g/l) TS and 1.5 ml of hydrochloric acid (~420 g/l) TS. Again evaporate to dryness; an orange-coloured residue is produced. Dissolve the residue in 0.5 ml of water and add 0.5 ml of ammonium chloride (100 g/l) TS; a yellow, crystalline precipitate is produced.

COAL TAR

Composition. Coal tar is a by-product usually obtained during the destructive distillation of coal. It is a complex and undefined mixture of a great number of chemical compounds. The product is available in various compositions.

Identity tests

Description. Brown-black or black, viscous liquid; odour, characteristic and strong, resembling naphthalene. On exposure to air the liquid solidifies.

Heating behaviour. When ignited, the liquid burns in air with a luminous sooty flame and almost no residue remains.

Colour and other reactions

1. Shake 1 drop vigorously with 5 ml of ethanol (~750 g/l) TS and filter; the filtrate is yellow with a bluish green fluorescence.
2. Shake about 1 g vigorously with 9 ml of water for 10 minutes and filter; the filtrate gives a neutral or only slightly acid reaction when tested with litmus paper R (unlike wood tar) and an odour of naphthalene is discernible (keep the filtrate for test 3).
3. To 5 ml of the filtrate from test 2 add a few drops of bromine TS; a yellow turbidity develops (phenols).

Degradation test

If the substance does not pass the following test, this usually indicates that gross degradation has occurred:

Dissolve 0.10 g in 10 ml of nitrobenzene R; a clear or almost clear solution is produced.

DOXORUBICIN HYDROCHLORIDE

Identity tests

Description. A red-orange, crystalline powder; hygroscopic.

Note. **This substance is very toxic and should be handled with care.**

Colour and other reactions

1. Place a small quantity of the test substance on a white test plate and add 1 drop of formaldehyde/sulfuric acid TS; the orange-red colour of the substance changes to violet.