BASIC TESTS FOR DRUGS

Pharmaceutical substances, medicinal plant materials and dosage forms

World Health Organization
Geneva
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