Farmakopeaseminaarisarja
Miten käytän farmakopeaa laboratoriossa?

Tuula Hauta-aho
Laboratoriopäällikkö
Analyyttinen laboratorio

Yliopiston Apteekki

Tuula Hauta-aho
FM (HY, orgaaninen kemia)
laboratoriopäällikkö
Yliopiston apteekin analyyttinen laboratorio

Työkokemusta yli 30 v. lääketeollisuudesta
GMP-laboratorioissa:
Fermion, Orion, YA, Fimea (1v)

Farmakopeakomitean jäsenyys 2010 ->

Koirakävely, puutarhanhoito, avovesiuinti

YA Yliopiston Apteekki

Hieman Yliopiston Apteekin analyyttisestä laboratoriosta..

- Osoite: Valimotie 7, Helsinki Pitäjänmäki
- Henkilökunta:
    - kemisti
    - 5 laboranttia
    - laboratorioanalyytikko
    - välinehuoltaja
- Apteekin analyyttinen laboratorio
- Fimean myöntämä GMP-lupa kemiallisten sopimusanalyysipalvelujen tuottamiseen lääketeollisuudelle vuodesta 2007

Esityksestä:

- 5.26. implementation of pharmacopoeial procedures
- Monografia paracetamol
- General monographs
  - Substances for pharmaceutical use (2034)
  - Pharmaceutical preparations (2619)
- Monografia paracetamol
  - Toteaminen -> IR (2.2.24.)
  - Sukulaisaineet -> HPLC (2.2.26)
    - Epäpuhtaudet
    - Pitoisuus

5.26. IMPLEMENTATION OF PHARMACOPOEIAL PROCEDURES

General Notices apply to all monographs and other texts.
See the information section on general monographs.

01/2023:52600

5.26. IMPLEMENTATION OF PHARMACOPOEIAL PROCEDURES

This general chapter is published for information. It provides guidance on setting up an approach for the implementation of analytical procedures given in monographs of the Ph. Eur. (or 'pharmacopoeial procedures' hereinafter). The approach set out below is valid only when used in accordance with the principles laid down in the General Notices (including a suitable quality system). The term "implementation" is used to describe the overall activities performed, whereas "verification" is used exclusively to refer to the experimental activities.

Approaches other than the one set forth in this general chapter may also be appropriate to ensure successful implementation. Ultimately, the implementation process runs under the user's responsibility and its successful outcome needs to be demonstrated and documented to the satisfaction of the competent authority.

INTRODUCTION

Implementation of a pharmacopoeial procedure is the process of demonstrating its suitability and applying it under the actual conditions of use in the implementing laboratory.

Pharmacopoeial procedures have been validated in accordance with accepted scientific practice and current recommendations on analytical validation (see Ph. Eur. General Notices). Therefore, unless otherwise stated, validation is not required when implementing these procedures. However, as also indicated in the General Notices, the user must assess whether and to what extent the suitability of the pharmacopoeial procedure under the actual conditions of use needs to be demonstrated in compliance with relevant monographs, general chapters and quality systems.

The chapter covers all types of analytical procedures given in Ph. Eur. monographs.

IMPLEMENTATION PROCESS

As the first step of the implementation process, an assessment is performed prior to the first use of the pharmacopoeial procedure in the implementing laboratory. The purpose of this assessment is not to evaluate the intrinsic capability of the procedure, but to determine whether there are any factors associated with the complexity of the procedure and the actual conditions of its use in the implementing laboratory that may affect the performance of the procedure.

If such factors are identified, an experimental verification is the second step to evaluate the analytical procedure performance characteristics (APPCs), such as accuracy and precision, that are considered relevant.

The publication of a revised monograph requires re-evaluation of the implementation of the concerned analytical procedure.

KNOWLEDGE DATABASE
5.26. IMPLEMENTATION OF PHARMACOPOEIAL PROCEDURES
ADDITIONAL INFORMATION

5.26. IMPLEMENTATION OF PHARMACOPOEIAL PROCEDURES (52600)

Examples of implementation of pharmacopoeial procedures according to Chapter 5.26
"*Implementation of pharmacopoeial procedures*"

English version is available at:
https://go.edqm.eu/ExamplesImplementation52600

KNOWLEDGE DATABASE
5.26. IMPLEMENTATION OF PHARMACOPOEIAL PROCEDURES
ADDITIONAL INFORMATION,

IMPLEMENTATION EXAMPLES

Content

KNOWLEDGE DATABASE
5.26. IMPLEMENTATION OF PHARMACOPOEIAL PROCEDURES
ADDITIONAL INFORMATION, RELATED SUBSTANCES TEST BY LC-UV

Verification plan and experiments

Experimental verification of the analytical procedure performance characteristics (APPCs) potentially affected by the factors identified during the assessment and based on recommended APPCs according to Ph.Eur. general text *5.26*.

SPECIFICITY/SELECTIVITY:

- Different test material – will need to ensure that the excipients do not contribute peaks that interfere with the active substance or impurities
  - Inject excipients to demonstrate non-interference
- Different source of reagents, e.g., mobile phase, different column (containing a similar stationary phase in terms of substituents and physico-chemical characteristics) and HPLC system
  - Blank injection
  - Elution order according to monograph (relative retentions are given for information)
  - System suitability criteria according to monograph and general chapter *2.2.46*

REPEATABILITY (PRECISION):

- Assess repeatability
  - Dilution of test solutions to obtain either API or impurity B at ~ 0.10%, preferably use a dilution of the test solution. Reference solution (a) contains 0.10% of the nominal sample concentration
  - 6 determinations

ACCURACY:

- All differences identified could result in different systematic errors and thus different biases at the implementing lab. However, none of the potential sources of systematic error is considered likely to be significant.
  - No verification experiments are required.

SENSITIVITY:

- Differences in HPLC system/detectors could affect the sensitivity of the analytical procedure in the implementing lab
- Confirm adequate signal to noise ratio at the reporting threshold
  - Sensitivity test should be included in SST according to Ph. Eur. general chapter *2.2.46*

Paracetamol

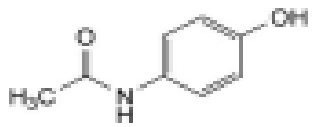
Document en Français | PDF | Knowledge Database

General Notices apply to all monographs and other texts
See the information section on general monographs.

04/2022:0049

PARACETAMOL

Paracetamolum



$C_8H_9NO_2$ M_r 151.2
[103-90-2]

DEFINITION

N-(4-Hydroxyphenyl)acetamide.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: sparingly soluble in water, freely soluble in ethanol (96 per cent), very slightly soluble in methylene chloride.

General monographs

GENERAL MONOGRAPHS

Whenever a monograph is used, it is essential to ascertain whether there is a general monograph applicable to the product in question.

The European Pharmacopoeia contains a number of general monographs covering classes of products. These general monographs give requirements that are applicable to all products in the given class or, in some cases, to any product in the given class for which there is a specific monograph in the Pharmacopoeia (see *1. General Notices*, General monographs). Where no restriction on the scope of a general monograph is given in a preamble, it is applicable to all products in the class defined, irrespective of whether there is an individual monograph for the product in the Pharmacopoeia.

The general monographs listed below are published in the General monographs section (unless otherwise stated). This list is updated where necessary and republished in each supplement.

Allergen products (1063)

Chemical precursors for radiopharmaceutical preparations (2902)

Dosage Forms
(published in the Dosage forms section or the Homoeopathic preparations section, as appropriate)

Essential oils (2098)

Herbal drug extracts (0765)

Herbal drug preparations (1434)

Herbal drugs (1433)

Herbal drugs for homoeopathic preparations (2045)
(published in the Homoeopathic preparations section)

Herbal teas (1435)

Herbal teas, instant (2620)

Homoeopathic preparations (1038)
(published in the Homoeopathic preparations section)

Immunosera for human use, animal (0084)

Immunosera for veterinary use (0030)

Live biotherapeutic products for human use (3053)

Methods of preparation of homoeopathic stocks and potentisation (2371)
(published in the Homoeopathic preparations section)

Monoclonal antibodies for human use (2031)

Mother tinctures for homoeopathic preparations (2029)
(published in the Homoeopathic Preparations section)

Pharmaceutical preparations (2619)

Products of fermentation (1468)

Products with risk of transmitting agents of animal spongiform encephalopathies (1483)

Radiopharmaceutical preparations (0125)

Recombinant DNA technology, products of (0784)

Substances for pharmaceutical use (2034)

Vaccines for human use (0153)

Vaccines for veterinary use (0062)

Vegetable fatty oils (1579)

SUBSTANCES FOR PHARMACEUTICAL USE
01/2021:2034

Elemental impurities. Permitted daily exposures for elemental impurities (e.g. as included in the ICH Q3D guideline, the principles of which are reproduced in general chapter 5.20. *Elemental impurities*) apply to the medicinal product. Individual monographs on substances for pharmaceutical use therefore do not contain specifications for elemental impurities unless otherwise prescribed.

Residual solvents are limited according to the principles defined in chapter 5.4, using general method 2.4.24 or another suitable method. Where a quantitative determination of a residual solvent is carried out and a test for loss on drying is not carried out, the content of residual solvent is taken into account for calculation of the assay content of the substance, the specific optical rotation and the specific absorbance.

Microbiological quality. Individual monographs give acceptance criteria for microbiological quality wherever such control is necessary. Table 5.1.4.-2. – *Acceptance criteria for microbiological quality of non-sterile substances for pharmaceutical use* in chapter 5.1.4. *Microbiological quality of non-sterile pharmaceutical preparations and substances for pharmaceutical use* gives recommendations on microbiological quality that are of general relevance for substances subject to microbial contamination. Depending on the nature of the substance and its intended use, different acceptance criteria may be justified.

Sterility (2.6.1). If intended for use in the manufacture of sterile dosage forms without a further appropriate sterilisation procedure, or if offered as sterile grade, the substance for pharmaceutical use complies with the test for sterility.

Bacterial endotoxins (2.6.14). The substance for pharmaceutical use complies with the test for bacterial endotoxins if it is labelled as a bacterial endotoxin-free grade or if it is intended for use in the manufacture of parenteral preparations or preparations for irrigation without a further appropriate procedure for the removal of bacterial endotoxins. The limit, when not indicated in the individual monograph, is determined in accordance with the recommendations of general chapter 5.1.10. *Guidelines for using the test for bacterial endotoxins*.

Pyrogens (2.6.8). If the test for pyrogens is justified rather than the test for bacterial endotoxins and if a pyrogen-free grade is offered, the substance for pharmaceutical use complies with the test for pyrogens. The limit and test method are stated in the individual monograph or approved by the competent authority. Based on appropriate test validation for bacterial endotoxins and pyrogens, the test for bacterial endotoxins may replace the test for pyrogens.

Additional properties. Control of additional properties (e.g. physical characteristics, functionality-related characteristics) may be necessary for individual manufacturing processes or formulations. Grades (such as sterile, endotoxin-free, pyrogen-free) may be produced with a view to manufacture of preparations for parenteral administration or other dosage forms and appropriate requirements may be specified in an individual monograph.

ASSAY

Unless justified and authorised, contents of substances for pharmaceutical use are determined. Suitable methods are used.

Paracetamol, toteaminen

IDENTIFICATION

First identification: B.

Second identification: A.

A. Melting point (*2.2.14*).

Determination A: determine the melting point of the substance to be examined.

Result A: 168 °C to 172 °C.

Determination B: mix equal parts of the substance to be examined and *paracetamol CRS* and determine the melting point of the mixture.

Result B: the absolute difference between the melting point of the mixture and the value obtained in determination A is not greater than 2 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *paracetamol CRS*.

2.2.24. ABSORPTION SPECTROPHOTOMETRY, INFRARED

METHODS

Infrared spectroscopy is mostly used to identify substances, but it may also be carried out for quantitative applications. Quantitative analysis (based on the Beer-Lambert law, which relates the absorbance of a sample to its concentration) will not be described in this chapter.

The measurement is performed on an appropriately prepared sample. The data is then processed and evaluated, either to identify substances or quantify them (e.g. based on integration of IR-absorption bands).

Spectral quality may be enhanced by mathematical pretreatments. In practice, these are limited to spectral normalisation and subtraction of bands caused by carbon-dioxide and water vapour. The same pretreatments are performed on both the sample and the reference spectra.

Identification

Prepare the substance to be examined appropriately and record the spectra between 4000 and 650 cm^{-1}, unless otherwise prescribed.

Identification testing is performed by comparing the spectrum of the substance to be examined with the spectrum obtained from a Ph. Eur. chemical reference substance (CRS) or with a Ph. Eur. reference spectrum.

The spectrum of the current batch of the Ph. Eur. CRS may be recorded for immediate use or stored, for example, in a spectral library for future consultation. A stored spectrum may be used, provided traceability to the current batch of CRS is ensured.

In the case of substances that are not covered by individual monographs, a suitable reference standard may be used.

In all cases, spectra must be recorded using the same operating conditions and procedure, and especially the same measurement mode.

When comparison of the spectra recorded in the solid state show differences (see below), treat the substance to be examined and the reference substance in the same manner so that they recrystallise or are produced in the same crystalline form, or proceed as prescribed in the monograph, then record the spectra again. However, this procedure must only be done for substances where the monograph does not cover a particular form of a substance that exhibits polymorphism.

Several comparison procedures may be used, and the analyst must document and justify the method used and the specific acceptance criteria that allow a conclusion for identification. The spectra can be compared either by overlaying the spectra (in the whole spectral range or in the region of interest specified in the monograph) or by using mathematical calculations from the software. It is possible for example to perform:

- visual comparison based on band positions and relative intensities unless otherwise specified - the transmission minima (or absorption maxima) in the spectrum obtained with the substance to be examined correspond in position and relative size to those of the reference;
- calculation of the correlation coefficient between the 2 spectra - this value is calculated by the software and the identification threshold is defined by the user;
- evaluation by chemometric methods (e.g. Euclidean distance, Mahalanobis distance, classification methods); these methods involve the set-up, assessment and validation of the chemometric model by the analyst (see 5.21. *Chemometric methods applied to analytical data*).

Paracetamol, sukulaisaineet

Related substances. Liquid chromatography (*2.2.29*).

Solvent mixture: *methanol R*, *water R* (15:85 *V/V*).

Test solution. Dissolve 50.0 mg of the substance to be examined in 0.75 mL of *methanol R* and dilute to 5.0 mL with *water R*.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 20.0 mL with the solvent mixture.

Reference solution (b). Dissolve 5.0 mg of *paracetamol impurity J CRS* in 25 mL of *methanol R* and dilute to 250.0 mL with the solvent mixture. Dilute 1.0 mL of the solution to 200.0 mL with the solvent mixture.

Reference solution (c). Dissolve 5.0 mg of *paracetamol impurity K CRS* in the solvent mixture and dilute to 100.0 mL with the solvent mixture. Dilute 1.0 mL of the solution to 10.0 mL with the solvent mixture.

Reference solution (d). Dilute 1.0 mL of reference solution (c) to 10.0 mL with the solvent mixture.

Reference solution (e). Mix 1 mL of reference solution (a) and 1 mL of reference solution (c) and dilute to 10 mL with the solvent mixture.

Column:

- *size*: *l* = 0.15 m, Ø = 4.6 mm;
- *stationary phase*: *end-capped solid core octadecylsilyl silica gel for chromatography R* (5 µm);
- *temperature*: 30 °C.

Mobile phase:

- *mobile phase A*: dissolve 1.7 g of *potassium dihydrogen phosphate R* and 1.8 g of *dipotassium hydrogen phosphate R* in *water for chromatography R* and dilute to 1000 mL with the same solvent;
- *mobile phase B*: *methanol R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 1.5	95	5
1.5 - 14.4	95 → 90	5 → 10
14.4 - 28.8	90	10
28.8 - 57.6	90 → 66	10 → 34
57.6 - 60	66	34

Flow rate: 1.5 mL/min.

Detection: spectrophotometer at 254 nm.

Autosampler: set at 5 °C.

Injection: 50 µL of the test solution and reference solutions (a), (b), (d) and (e).

Identification of impurities: use the chromatogram obtained with reference solution (b) to identify the peak due to impurity J; use the chromatogram obtained with reference solution (d) to identify the peak due to impurity K.

Relative retention with reference to paracetamol (retention time = about 4 min): impurity K = about 0.4; impurity J = about 10.1.

System suitability: reference solution (e):

- *resolution*: minimum 5.0 between the peaks due to impurity K and paracetamol.

Calculation of contents:

- for impurity J, use the concentration of impurity J in reference solution (b);
- for impurity K, use the concentration of impurity K in reference solution (d);
- for impurities other than J and K, use the concentration of paracetamol in reference solution (a).

Limits:

- *impurity K*: maximum 50 ppm;
- *impurity J*: maximum 10 ppm;
- *unspecified impurities*: for each impurity, maximum 0.05 per cent;
- *total*: maximum 0.2 per cent;
- *reporting threshold*: 0.03 per cent, except for impurities J and K.

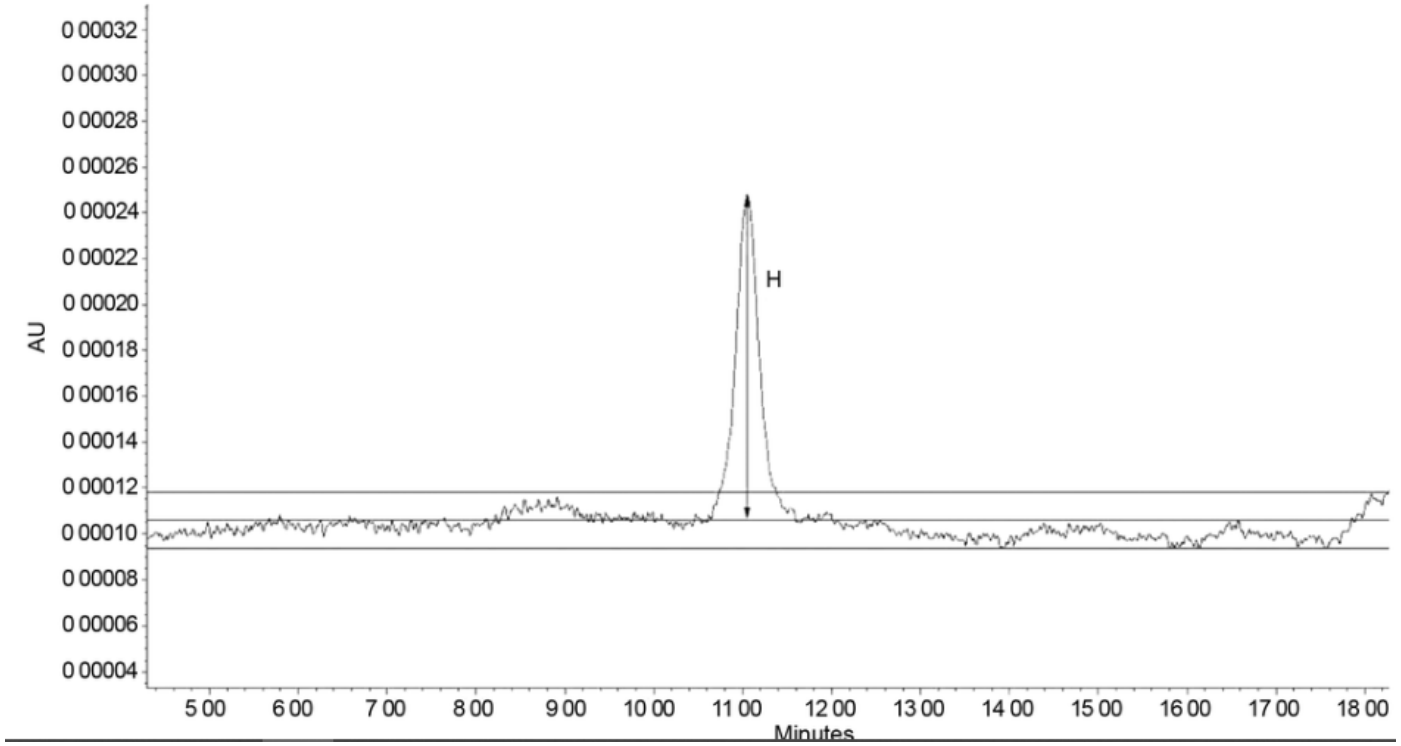
2.2.46. CHROMATOGRAPHIC SEPARATION TECHNIQUES

Signal-to-noise ratio (*S/N*)[2] (IMPORTANT INFO)

Short-term noise influences the precision and accuracy of quantitation. The signal-to-noise ratio is calculated using the following equation:

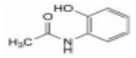
$$S/N = \frac{2H}{h}$$

H	=	height of the peak (Figure 2.2.46.-6) corresponding to the component concerned, in the chromatogram obtained with the reference solution, measured from the maximum of the peak to the extrapolated baseline of the signal observed over a distance equal to 20 times the width at half-height;
h	=	range of the noise in a chromatogram obtained after injection of a blank (Figure 2.2.46.-7), observed over a distance equal to 20 times the width at half-height of the peak in the chromatogram obtained with the reference solution and, if possible, situated equally around the place where this peak would be found.

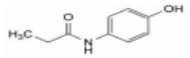


Paracetamol, impurities

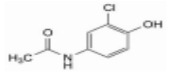
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): *A, B, C, D, E, F, G, H, I, L, M, N, O.*



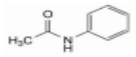
A. *N*-(2-hydroxyphenyl)acetamide,



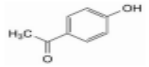
B. *N*-(4-hydroxyphenyl)propanamide,



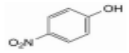
C. *N*-(3-chloro-4-hydroxyphenyl)acetamide,



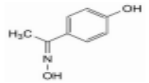
D. *N*-phenylacetamide,



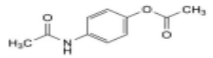
E. 1-(4-hydroxyphenyl)ethan-1-one,



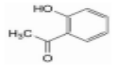
F. 4-nitrophenol,



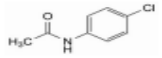
G. [1-(4-hydroxyphenyl)ethylidene]hydroxylamine,



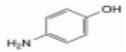
H. 4-acetamidophenyl acetate,



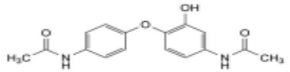
I. 1-(2-hydroxyphenyl)ethan-1-one,



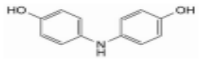
J. *N*-(4-chlorophenyl)acetamide (chloroacetanilide),



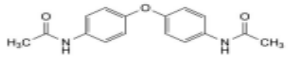
K. 4-aminophenol,



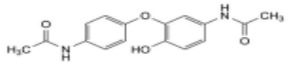
L. *N*-[4-(4-acetamido-2-hydroxyphenoxy)phenyl]acetamide,



M. 4,4′-azanediyldiphenol,



N. *N*,*N*′-[oxydi(4,1-phenylene)]diacetamide,



O. *N*-[4-(5-acetamido-2-hydroxyphenoxy)phenyl]acetamide.

01/2008:1034

PARAFFIN, HARD

Paraffinum solidum

DEFINITION

A purified mixture of solid saturated hydrocarbons generally obtained from petroleum. It may contain a suitable antioxidant.

CHARACTERS

Appearance: colourless or white or almost white mass; the melted substance is free from fluorescence in daylight.
Solubility: practically insoluble in water, freely soluble in methylene chloride, practically insoluble in ethanol (96 per cent).

IDENTIFICATION

First identification: *A, C.*
Second identification: *B, C.*

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *hard paraffin CRS.*
Preparation: place about 2 mg on a sodium chloride plate, heat in an oven at 100 °C for 10 min, spread the melted substance with another sodium chloride plate and remove one of the plates.

B. Acidity or alkalinity (see Tests).

C. Melting point (*2.2.16*): 50 °C to 61 °C.

TESTS

Acidity or alkalinity. To 15 g add 30 mL of boiling *water R* and shake vigorously for 1 min. Allow to cool and to separate. To 10 mL of the aqueous layer add 0.1 mL of *phenolphthalein solution R*. The solution is colourless. Not more than 1.0 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to red. To a further 10 mL of the aqueous layer

paracetamol

Detailed view of Paracetamol.

Status	In use
Monograph Number	00049
English Name	Paracetamol
French Name	Paracétamol
Latin Name	Paracetamolum
Pinyin Name	
Chinese Name	
Pharmeuropa	32.1
Published in English Supplement	10.7
Published in French Supplement	10.7
Chromatogram	Available
Additional information	Not available
History	View history
Interchangeable (ICH_Q4B)	NO
Pharmacopoeial harmonisation	NO

Reference standards

Available since	Cat. No.	Name	Batch No.	Unit Quantity	Price
	P0300000	Paracetamol CRS	4	50 mg	79 EUR
	Y0001945	Paracetamol impurity J CRS	2	15 mg	79 EUR
	Y0001955	Paracetamol impurity K CRS	1	15 mg	79 EUR

Practical Information

Test(s)	Brand Name/Information
Related substances	Halo C18 is suitable. D0 (Dwell volume used for the development of the analytical procedure) = 1.13mL.

Monograph Number	Substance	Type CEP	Certificate (CEP) Holder	Holder SPOR ORG-ID SPOR LOC-ID	Certificate (CEP) Number	Issue Date CEP	Status CEP
49	Paracetamol	Chemical	Indukern Chemie AG Schlieren CH		R0-CEP 2000-002 - Rev 00	22/10/2001	Withdrawn by EDQM Failure to CEP procedure

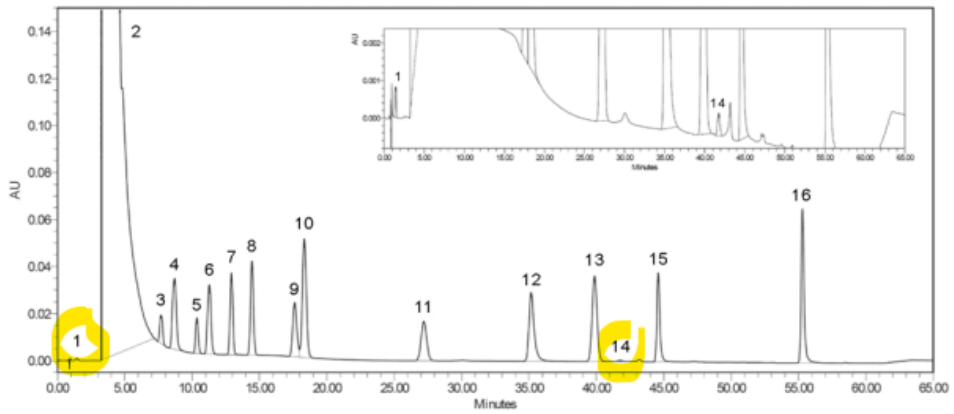
Knowledge database, Chromatogram

04/2022:0049

PARACETAMOL

Paracetamolum

The following chromatogram is shown for information but will not be published in the European Pharmacopoeia.



1. impurity K	5. impurity F	9. impurity M	13. impurity I
2. paracetamol	6. impurity C	10. impurity G	14. impurity J
3. impurity A	7. impurity D	11. impurity H	15. impurity L
4. impurity B	8. impurity E	12. impurity O	16. impurity N

Figure 0049.-1. – *Chromatogram for the test for related substances of paracetamol: test solution spiked with impurities A to O (A, B, C, D, E, F, G, H, I, L, M, N, O at 0.05 per cent, K at 50 ppm, and J at 10 ppm)*

Knowledge database, reference substances, leaflet

INFORMATION LEAFLET Ph. Eur. Reference Standard

PARACETAMOL CRS batch 4

1. **Identification**

Catalogue code: P0300000 Unit Quantity: ca 50 mg

2. **Scientific Information**

2.1 Intended use

Reference Standard for laboratory tests as prescribed in the European Pharmacopoeia only.
Established for use with the monograph(s): 0049.

2.2 Analytical information related to intended use, when applicable

2.3 Uncertainty of the assigned value, when applicable

The uncertainty of the assigned value is not stated since it is considered to be negligible in relation to the defined limits of the method-specific assays for which the reference standard is used. Please also refer to Ph. Eur. chapter 5.12.

2.4 Validity

Ph. Eur. RS are periodically tested to ensure their continuous fitness for purpose. For each valid Ph. Eur. RS, a Batch Validity Statement at the time of use can be downloaded and printed from the EDQM website (Reference Standards Database).

2.5 Instructions for use

The container should not be opened until required for use. Allow the closed container to equilibrate at ambient temperature before opening to avoid uptake of moisture. Use "as is". Do not dry/desiccate before use. Ph. Eur. RS are for immediate use. Once the container has been opened, its entire content must be used immediately. Any further storage and re-use are not warranted.

3. **Storage conditions**

In the original container at +5°C ± 3°C, protected from light. Re-instate promptly upon receipt.

paracetamol

Loss on drying (2.2.32): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (2.4.14): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.300 g in a mixture of 10 mL of water R and 30 mL of dilute sulfuric acid R. Boil under a reflux condenser for 1 h, cool and dilute to 100.0 mL with water R. To 20.0 mL of the solution add 40 mL of water R, 40 g of ice, 15 mL of dilute hydrochloric acid R and 0.1 mL of ferroin R. Titrate with 0.1 M cerium sulfate until a greenish-yellow colour is obtained. Carry out a blank titration.

1 mL of 0.1 M cerium sulfate is equivalent to 7.56 mg of $C_8H_9NO_2$.

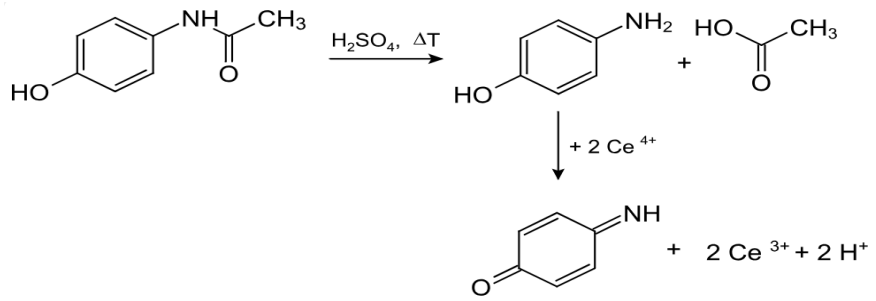
STORAGE

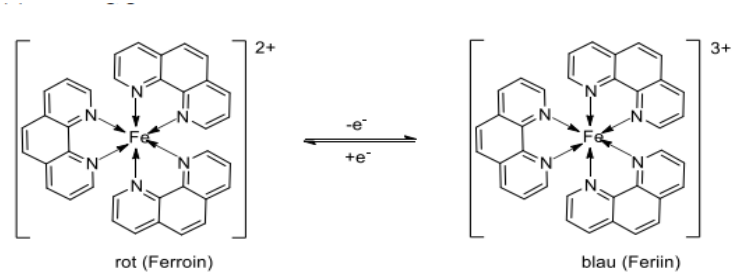
Protected from light.

Pitoisuus, titraus Cerium(IV) sulfaatilla

1. Paracetamolin hydrolyysi 4-aminophenoliksi: kuumennus rikkihapolla
2. 4-aminofenolin hapetus p-iminokinoniksi, cerium(IV)sulfaatti
3. kun kaikki hapettunut ferroiini (punainen) hapettuu feriiniksi (sininen)
4. 1 mol Ce4+ kuluttaa 0,5 mol paracetamolia
(1 ml 0,1M cerium sulfate is equivalent to 7,56 mg of C8H9NO2) mp 151,2 g/mol

Lähde: Arzneibuch-Kommentar zur Ph.Eur. (Govi-verlag)





Yliopiston Apteekki

♡ Tuottomme käytetään koulutukseen ja tutkimukseen

SINUA VARTEN VUODESTA 1755