How to use the BP

Getting started

If a drug product is licensed in a country where the BP is a legal standard:

• it should be able to comply with the requirements of the BP at any time throughout its shelf life
• it should meet the standards of the BP regardless of whether compliance with the BP is claimed or it is not called by the name at the head of the monograph

For a drug product to be compliant with a BP monograph:

• the monograph that was in force at the date of product manufacture should be applied e.g. BP 2019 is legally effective between 01/01/2019 and 31/12/2019. The effective date can be found in the Introduction section of the BP
• all ingredients (drug substances and excipients) that are used to make the product should comply with the published BP or Ph. Eur. monograph for those substances
• the product should comply with the relevant general monographs
• the product should comply with the requirements of the monograph for the formulated preparation

What you should do if:

• you have developed a method which is an improvement on the current BP procedure and want to propose a revision to the monograph
• you believe that there is an error in the BP

Contact bpcom@mhra.gov.uk with the information needed to contribute to monograph development (described on the Monograph Development page on the BP website) or, providing details of the error with data if appropriate.

Navigating the BP

The BP is the only comprehensive collection of authoritative official standards for UK pharmaceutical substances and medicinal products, it contains all texts and monographs of the European Pharmacopoeia (signposted with a chaplet of stars) as well as the national standards developed by the BP. Unsurprisingly, this means the BP contains a lot of text and information. Over the next pages there is a guide to finding your way around the BP:
How to use the BP: Following a monograph

This guide is designed to provide broad explanations of how to apply a BP monograph and uses the BP 2019 Aspirin Tablets monograph as the example.

**Aspirin Tablets**

**General Notices**

The tablets comply with the requirements stated under Tablets and with the following requirements.

**Content of aspirin, C$_9$H$_8$O$_4$**

95.0 to 105.0% of the stated amount

**IDENTIFICATION**

Shake a quantity of the powdered tablets containing 0.5 g of Aspirin with 20 mL of absolute ethanol, filter (Whatman GF/C is suitable), evaporate the filtrate and dry the residue at 60° for 1 hour. The infrared absorption spectrum of the residue, is concordant with the reference spectrum of aspirin (RS 483).

**TESTS**

**Dissolution**

Comply with the requirements for Monographs of the British Pharmacopoeia in the dissolution test for tablets and capsules, Appendix XII B1.

**TEST CONDITIONS**

(a) Use Apparatus 1, rotating the basket at 50 revolutions per minute.

(b) Use 500 mL of a pH 4.5 buffer prepared by mixing 29.9 g of sodium acetate and 16.6 mL of glacial acetic acid with sufficient water to produce 10 litres at a temperature of 37°, as the medium.
PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and measure the absorbance of the filtered sample, suitably diluted with the dissolution medium if necessary, at the maximum at 265 nm, Appendix II B using dissolution medium in the reference cell.

(2) Measure the absorbance of a suitable solution of aspirin BPCRS using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of aspirin, C₉H₈O₄, in the medium using the declared content of C₉H₈O₄ in aspirin BPCRS.

Related substances

Carry out the method for liquid chromatography, Appendix III D, using the following solutions prepared immediately before use.

(1) Mix with the aid of ultrasound for 15 minutes a quantity of the powdered tablets containing 0.10 g of Aspirin with 40 mL of acetonitrile, allow to cool, dilute to 100 mL with water and filter through a 0.45-µm PTFE filter.

(2) Dilute 1 volume of solution (1) to 50 volumes and further dilute 1 volume of the resulting solution to 10 volumes with the mobile phase.

(3) 0.003% w/v of salicylic acid (impurity C) in the mobile phase.

(4) 0.1% w/v of aspirin impurity standard BPCRS in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with octadecylsilyl silica gel for chromatography (5 µm) (Kromasil C18 is suitable).

(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 1.0 mL per minute.

(d) Use an ambient column temperature.

(e) Use a detection wavelength of 237 nm.

(f) Inject 20 µL of each solution.

(g) Allow the chromatography to proceed for 1.2 times the retention time of impurity F.

Where there is no ‘Limits’ section following ‘Determination of content’ in the monograph, check section 3.4 of Supplementary Chapter I E Dissolution Testing of Solid Oral Dosage Forms. If the monograph title is listed here, apply a limit of not less than 70% of the label claim in 45 minutes. If the monograph is not listed in SC I E, follow the decision tree in section 3.3 of the same supplementary chapter.

This test is designed to provide limits for potential impurities related to the drug substance, rather than all possible impurities such as adulterants or contaminants.

BPCRS Information Leaflets can be a good source of guidance e.g. reference chromatograms. Information leaflets are available free of charge in the online reference standards catalogue: https://www.pharmacopoeia.com/Catalogue/Products. Reference material with the suffix EPCRS and CRS can be obtained from the European Directorate for the Quality of Medicines & HealthCare (EDQM): https://www.edqm.eu/en/ph-eur-reference-standards-orders-catalogue.

Appendix III Chromatographic Separation Techniques includes details on making adjustments to chromatographic conditions.

The General Notices require that, unless stated otherwise, Assays and tests are performed between 15 to 25 °C. Ambient temperature should be taken to mean between 15 to 25 °C.
MOBILE PHASE
2 volumes of orthophosphoric acid, 400 volumes of acetonitrile and 600 volumes of water.

When the chromatograms are recorded under the prescribed conditions, the retention times relative to aspirin (retention time about 5 minutes) are: impurity A, about 0.6; impurity B, about 0.7, impurity C, about 1.4 and impurity F, about 8.0.

SYSTEM SUITABILITY
The test is not valid unless, in the chromatogram obtained with solution (4) the resolution between the peaks due to aspirin and impurity C is at least 6.

LIMITS
In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity C is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (3%);
the area of any other secondary peak is not greater than half of the area of the principal peak in the chromatogram obtained with solution (2) (0.1%);
the sum of the areas of any other secondary peaks is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (1.0%).

Disregard any peak with an area less than 0.25 times the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY
Weigh and powder 20 tablets. Carry out the method for liquid chromatography, Appendix III D, using the following solutions prepared immediately before use.

(1) Mix with the aid of ultrasound for 15 minutes a quantity of the powdered tablets containing 60 mg of Aspirin with 40 mL of acetonitrile, allow to cool, dilute to 100 mL with water and filter through a 0.45-µm PTFE filter.

(2) 0.06% w/v of aspirin BPCRS in the mobile phase.

(3) 0.1% w/v of aspirin impurity standard BPCRS in the mobile phase.
CHROMATOGRAPHIC CONDITIONS
The chromatographic procedure described under Related substances may be used.

SYSTEM SUITABILITY
The test is not valid unless, in the chromatogram obtained with solution (3) the resolution between the peaks due to aspirin and impurity C is at least 6.0.

DETERMINATION OF CONTENT
Calculate the content of C9H8O4 in the tablets from the chromatograms obtained using the declared content of C9H8O4 in aspirin BPCS.

LABELLING
The label states that the tablets contain Aspirin, unless this word appears in the name of the tablets. This requirement does not apply in countries where exclusive proprietary rights in the name Aspirin are claimed.

IMPURITIES
The impurities limited by the requirements of this monograph include those listed under Aspirin.

The declared content of a BPCS can be found in the online catalogue and in the leaflet.

Labelling requirements in monographs are not comprehensive and the requirements of the regulatory authority where the product is marketed should be met. More information on the status and interpretation of the labelling section can be found in Supplementary Chapter I G Labelling.

This means that the Related substances test can detect and control the impurities listed in the drug substance monograph for Aspirin (Ph. Eur. monograph 0309, Acetylsalicylic Acid).