Reference solution (b). Dissolve 2.0 mg of *bisacodyl for system suitability CRS* (containing impurities A, B, C, D and E) in 1.0 ml of *acetonitrile R* and dilute to 2.0 ml with the solvent mixture.

Reference solution (c). Dissolve 5.0 mg of *bisacodyl for peak identification CRS* (containing impurity F) in 2.5 ml of *acetonitrile R* and dilute to 5.0 ml with the solvent mixture.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *end-capped octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mix 45 volumes of *acetonitrile R* and 55 volumes of a 1.58 g/l solution of *ammonium formate R* previously adjusted to pH 5.0 with *anhydrous formic acid R*.

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 265 nm.

Injection: 20 µl.

Run time: 3.5 times the retention time of bisacodyl.

Identification of impurities: use the chromatogram supplied with *bisacodyl for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, B, C, D and E.

Relative retention with reference to bisacodyl (retention time = about 13 min): impurity A = about 0.2; impurity B = about 0.4; impurity C = about 0.45; impurity D = about 0.8; impurity E = about 0.9; impurity F = about 2.6.

System suitability: reference solution (b):

– *peak-to-valley ratio*: minimum 1.5, where H_p = height above the baseline of the peak due to impurity E and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

Limits:

– *correction factor*: for the calculation of content, multiply the peak area of impurity A by 0.7;

– *impurities A, B*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);

– *impurities C, E*: for each impurity, not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

– *impurity D*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);

– *impurity F*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent);

– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

– *total*: not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);

– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 0.500 g by drying in an oven at 105 °C.

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

ASSAY

Dissolve 0.300 g in 60 ml of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid* determining the end-point potentiometrically (*2.2.20*).

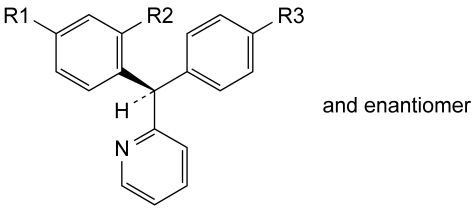
1 ml of *0.1 M perchloric acid* is equivalent to 36.14 mg of $C_{22}H_{19}NO_4$.

STORAGE

Protected from light.

IMPURITIES

Specified impurities: A, B, C, D, E, F.



and enantiomer

A. R1 = R3 = OH, R2 = H: 4,4′-(pyridin-2-ylmethylene)diphenol,

B. R1 = H, R2 = R3 = OH: 2-[(*RS*)-(4-hydroxyphenyl)(pyridin-2-yl)methyl]phenol,

C. R1 = OH, R2 = H, R3 = O-CO-CH_3: 4-[(*RS*)-(4-hydroxyphenyl)(pyridin-2-yl)methyl]phenyl acetate,

E. R1 = H, R2 = R3 = O-CO-CH_3: 2-[(*RS*)-[4-(acetyloxy)-phenyl](pyridin-2-yl)methyl]phenyl acetate,

D. unknown structure,

F. unknown structure.

01/2008:0012
corrected 6.0

BISMUTH SUBCARBONATE

Bismuthi subcarbonas

DEFINITION

Content: 80.0 per cent to 82.5 per cent of Bi (A_r 209.0) (dried substance).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water and in ethanol (96 per cent). It dissolves with effervescence in mineral acids.

IDENTIFICATION

A. It gives the reaction of carbonates (*2.3.1*).

B. It gives the reactions of bismuth (*2.3.1*).

TESTS

Solution S. Shake 5.0 g with 10 ml of *water R* and add 20 ml of *nitric acid R*. Heat to dissolve, cool and dilute to 100 ml with *water R*.

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*) and is colourless (*2.2.2, Method II*).

Chlorides (*2.4.4*): maximum 500 ppm.

To 6.6 ml of solution S add 4 ml of *nitric acid R* and dilute to 50 ml with *water R*.

Nitrates: maximum 0.4 per cent.

To 0.25 g in a 125 ml conical flask, add 20 ml of *water R*, 0.05 ml of *indigo carmine solution R1* and then, as a single addition but with caution, 30 ml of *sulphuric acid R*. Titrate immediately with *indigo carmine solution R1* until a stable blue colour is obtained. Not more than *n* ml of the titrant is required, *n* being the volume corresponding to 1 mg of NO_3.

Alkali and alkaline-earth metals: maximum 1.0 per cent.

To 1.0 g add 10 ml of *water R* and 10 ml of *acetic acid R*. Boil for 2 min, cool and filter. Wash the residue with 20 ml of *water R*. To the combined filtrate and washings add 2 ml of *dilute hydrochloric acid R* and 20 ml of *water R*. Boil and pass *hydrogen sulphide R* through the boiling solution until no further precipitate is formed. Filter, wash the residue with *water R*, evaporate the combined filtrate and washings to dryness on a water-bath and add 0.5 ml of *sulphuric acid R*. Ignite gently and allow to cool. The residue weighs a maximum of 10 mg.

Arsenic (*2.4.2, Method A*): maximum 5 ppm.

To 0.5 g in a distillation flask add 5 ml of *water R* and 7 ml of *sulphuric acid R*, allow to cool and add 5 g of *reducing mixture R* and 10 ml of *hydrochloric acid R*. Heat the contents of the flask to boiling gradually over 15-30 min and continue heating at such a rate that the distillation proceeds steadily until the volume in the flask is reduced by half or until 5 min after the air-condenser has become full of steam. It is important that distillation be discontinued before fumes of sulphur trioxide appear. Collect the distillate in a tube containing 15 ml of *water R* cooled in ice-water. Wash down the condenser with *water R* and dilute the distillate to 25 ml with the same solvent. Prepare the standard using a mixture of 2.5 ml of *arsenic standard solution (1 ppm As) R* and 22.5 ml of *water R*.

Copper: maximum 50 ppm.

To 5 ml of solution S, add 2 ml of *ammonia R* and dilute to 50 ml with *water R*. Filter. To 10 ml of the filtrate add 1 ml of a 1 g/l solution of *sodium diethyldithiocarbamate R*. The solution is not more intensely coloured than a standard prepared at the same time in the same manner using a mixture of 0.25 ml of *copper standard solution (10 ppm Cu) R* and 9.75 ml of *water R* instead of 10 ml of the filtrate.

Lead: maximum 20.0 ppm.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Dissolve 12.5 g in 75 ml of a mixture of equal volumes of *lead-free nitric acid R* and *water R*. Boil for 1 min, cool and dilute to 100.0 ml with *water R*.

Reference solutions. Prepare the reference solutions using appropriate quantities of lead standard solution and a 37 per cent *V/V* solution of *lead-free nitric acid R*.

Source: lead hollow-cathode lamp.

Wavelength: 283.3 nm (depending on the apparatus, the line at 217.0 nm may be used).

Atomisation device: air-acetylene flame.

Silver: maximum 25 ppm.

To 2.0 g add 1 ml of *water R* and 4 ml of *nitric acid R*. Heat gently until dissolved and dilute to 11 ml with *water R*. Cool and add 2 ml of *1 M hydrochloric acid*. Allow to stand protected from light for 5 min. Any opalescence in the solution is not more intense than that in a standard prepared at the same time in the same manner using a mixture of 10 ml of *silver standard solution (5 ppm Ag) R*, 1 ml of *nitric acid R* and 2 ml of *1 M hydrochloric acid*.

Loss on drying (*2.2.32*): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

ASSAY

Dissolve 0.500 g in 3 ml of *nitric acid R* and dilute to 250 ml with *water R*. Carry out the complexometric titration of bismuth (*2.5.11*).

1 ml of *0.1 M sodium edetate* is equivalent to 20.90 mg of Bi.

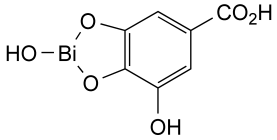
STORAGE

Protected from light.

01/2008:1493
corrected 6.0

BISMUTH SUBGALLATE

Bismuthi subgallas



$C_7H_5BiO_6$ M_r 394.1
[149-91-7]

DEFINITION

Complex of bismuth and gallic acid.

Content: 48.0 per cent to 51.0 per cent of Bi (A_r 209.0) (dried substance).

CHARACTERS

Appearance: yellow powder.

Solubility: practically insoluble in water and in alcohol. It dissolves in mineral acids with decomposition and in solutions of alkali hydroxides, producing a reddish-brown liquid.

IDENTIFICATION

A. Mix 0.1 g with 5 ml of *water R* and 0.1 ml of *phosphoric acid R*. Heat to boiling and maintain boiling for 2 min. Cool and filter. To the filtrate, add 1.5 ml of *ferric chloride solution R1*, a blackish-blue colour develops.

B. It gives reaction (b) of bismuth (*2.3.1*).

TESTS

Solution S. In a porcelain or quartz dish, ignite 1.0 g, increasing the temperature very gradually. Heat in a muffle furnace at 600 ± 50 °C for 2 h. Cool and dissolve the residue with warming in 4 ml of a mixture of equal volumes of *lead-free nitric acid R* and *water R* and dilute to 20 ml with *water R*.

Acidity. Shake 1.0 g with 20 ml of *water R* for 1 min and filter. To the filtrate add 0.1 ml of *methyl red solution R*. Not more than 0.15 ml of *0.1 M sodium hydroxide* is required to change the colour of the indicator to yellow.

Chlorides (*2.4.4*): maximum 200 ppm.

To 0.5 g add 10 ml of *dilute nitric acid R*. Heat on a water-bath for 5 min and filter. Dilute 5 ml of the filtrate to 15 ml with *water R*.