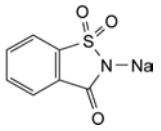
01/2008:0787

SACCHARIN SODIUM

Saccharinum natricum



$C_7H_4NNaO_3S$ M_r 205.2
[128-44-9]

DEFINITION

2-Sodio-1,2-benzisothiazol-3(2*H*)-one 1,1-dioxide.

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

It may contain a variable quantity of water.

CHARACTERS

Appearance: white or almost white, crystalline powder or colourless crystals, efflorescent in dry air.

Solubility: freely soluble in water, sparingly soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: B, E.

Second identification: A, C, D, E.

A. Melting point (*2.2.14*): 226 °C to 230 °C.

To 5 mL of solution S (see Tests) add 3 mL of *dilute hydrochloric acid R*. A white precipitate is formed. Filter and wash with *water R*. Dry the precipitate at 100-105 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs; dry the substances at 100-105 °C before use.

Comparison: *saccharin sodium CRS*.

C. Mix about 10 mg with about 10 mg of *resorcinol R*, add 0.25 mL of *sulfuric acid R* and carefully heat the mixture over a naked flame until a dark green colour is produced. Allow to cool, add 10 mL of *water R* and *dilute sodium hydroxide solution R* until an alkaline reaction is produced. An intense green fluorescence develops.

D. To 0.2 g add 1.5 mL of *dilute sodium hydroxide solution R*, evaporate to dryness and heat the residue carefully until it melts, avoiding carbonisation. Allow to cool, dissolve the mass in about 5 mL of *water R*, add *dilute hydrochloric acid R* until a weak acid reaction is produced and filter, if necessary. To the filtrate add 0.2 mL of *ferric chloride solution R2*. A violet colour develops.

E. Solution S gives reaction (a) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 5.0 g in *carbon dioxide-free water R* and dilute to 50.0 mL with the same solvent.

Appearance of solution. The solution is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Dissolve 5.0 g in 25 mL of *carbon dioxide-free water R*.

Acidity or alkalinity. To 10 mL of solution S add about 0.05 mL of a 10 g/L solution of *phenolphthalein R* in *ethanol (96 per cent) R*. The solution is not pink. Add 0.1 mL of *sodium hydroxide 0.1 M*. The solution becomes pink.

***o*- and *p*-Toluenesulfonamide**. Gas chromatography (*2.2.28*).

Internal standard solution. Dissolve 25 mg of *caffeine R* in *methylene chloride R* and dilute to 100 mL with the same solvent.

Test solution. Dissolve 10.0 g of the substance to be examined in 50 mL of *water R*. If necessary adjust the solution to pH 7-8 by addition of *1 M sodium hydroxide* or *1 M hydrochloric acid*. Shake the solution with 4 quantities, each of 50 mL, of *methylene chloride R*. Combine the lower layers, dry over *anhydrous sodium sulfate R* and filter. Wash the filter and the sodium sulfate with 10 mL of *methylene chloride R*. Combine the solution and the washings and evaporate almost to dryness in a water-bath at a temperature not exceeding 40 °C. Using a small quantity of *methylene chloride R*, quantitatively transfer the residue into a suitable 10 mL tube, evaporate to dryness in a current of *nitrogen R* and add 1.0 mL of the internal standard solution.

Blank solution. Evaporate 200 mL of *methylene chloride R* to dryness in a water-bath at a temperature not exceeding 40 °C. Dissolve the residue in 1 mL of *methylene chloride R*.

Reference solution. Dissolve 20.0 mg of *o-toluenesulfonamide R* and 20.0 mg of *p-toluenesulfonamide R* in *methylene chloride R* and dilute to 100.0 mL with the same solvent. Dilute 5.0 mL of the solution to 50.0 mL with *methylene chloride R*. Evaporate 5.0 mL of the final solution to dryness in a current of *nitrogen R*. Take up the residue using 1.0 mL of the internal standard solution.

Column:

- *material*: fused silica,
- *size*: *l* = 10 m, Ø = 0.53 mm,
- *stationary phase*: *polymethylphenylsiloxane R* (film thickness 2 µm).

Carrier gas: *nitrogen for chromatography R*.

Flow rate: 10 mL/min.

Split ratio: 1:2.

Temperature:

- *column*: 180 °C,
- *injection port and detector*: 250 °C.

Detection: flame ionisation.

Injection: 1 µL.

Elution order: *o*-toluenesulfonamide, *p*-toluenesulfonamide, caffeine.

System suitability:

- *resolution*: minimum 1.5 between the peaks due to *o*-toluenesulfonamide and *p*-toluenesulfonamide in the chromatogram obtained with the reference solution,
- the chromatogram obtained with the blank solution does not show any peak with the same retention times as the internal standard, *o*-toluenesulfonamide and *p*-toluenesulfonamide.

Limits:

- *o-toluenesulfonamide*: the ratio of its area to that of the internal standard is not greater than the corresponding ratio in the chromatogram obtained with the reference solution (10 ppm),
- *p-toluenesulfonamide*: the ratio of its area to that of the internal standard is not greater than the corresponding ratio in the chromatogram obtained with the reference solution (10 ppm).

Readily carbonisable substances. Dissolve 0.20 g in 5 mL of *sulfuric acid R* and keep at 48-50 °C for 10 min. When viewed against a white background, the solution is not more intensely coloured than a solution prepared by mixing 0.1 mL of red primary solution, 0.1 mL of blue primary solution and 0.4 mL of yellow primary solution (*2.2.2*) with 4.4 mL of *water R*.

Heavy metals (*2.4.8*): maximum 20 ppm.

12 mL of solution S complies with test A. Prepare the reference solution using *lead standard solution (2 ppm Pb) R*.

Water (*2.5.12*): maximum 15.0 per cent, determined on 0.200 g.

ASSAY

Dissolve 0.150 g in 50 mL of *anhydrous acetic acid R*, with slight heating if necessary. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*). Carry out a blank titration.

1 mL of *0.1 M perchloric acid* is equivalent to 20.52 mg of $C_7H_4NNaO_3S$.

STORAGE

In an airtight container.

01/2010:2088

SAFFLOWER OIL, REFINED

Carthami oleum raffinatum

DEFINITION

Fatty oil obtained from seeds of *Carthamus tinctorius* L. (type I) or from seeds of hybrids of *Carthamus tinctorius* L. (type II), by expression and/or extraction followed by refining. Type II refined safflower oil is rich in oleic (*cis*-9-octadecenoic) acid. A suitable antioxidant may be added.

CHARACTERS

Appearance: clear, viscous, yellow or pale yellow liquid.

Solubility: practically insoluble in ethanol (96 per cent), miscible with light petroleum (bp: 40-60 °C).

	Type I refined safflower oil	Type II refined safflower oil
Relative density	about 0.922	about 0.914
Refractive index	about 1.476	about 1.472

IDENTIFICATION

First identification: B.

Second identification: A.

A. Identification of fatty oils by thin-layer chromatography (*2.3.2*).

Results: the chromatogram obtained is similar to the corresponding chromatogram for type I or type II shown in Figure 2.3.2.-1.

B. Composition of fatty acids (see Tests).

TESTS

Acid value (*2.5.1*): maximum 0.5.

Peroxide value (*2.5.5, Method A*): maximum 10.0, or maximum 5.0 if intended for use in the manufacture of parenteral preparations.

Unsaponifiable matter (*2.5.7*): maximum 1.5 per cent, determined on 5.0 g.

Alkaline impurities (*2.4.19*). It complies with the test.

Composition of fatty acids (*2.4.22, Method A*). Use the mixture of calibrating substances in Table 2.4.22.-3.

Composition of the fatty-acid fraction of type I refined safflower oil:

- *saturated fatty acids of chain length less than C14*: maximum 0.2 per cent;
- *myristic acid*: maximum 0.2 per cent;
- *palmitic acid*: 4.0 per cent to 10.0 per cent;
- *stearic acid*: 1.0 per cent to 5.0 per cent;
- *oleic acid*: 8.0 per cent to 21.0 per cent;
- *linoleic acid*: 68.0 per cent to 83.0 per cent;
- *linolenic acid*: maximum 0.5 per cent;
- *arachidic acid*: maximum 0.5 per cent;
- *eicosenoic acid*: maximum 0.5 per cent;
- *behenic acid*: maximum 1.0 per cent.

Composition of the fatty-acid fraction of type II refined safflower oil:

- *saturated fatty acids of chain length less than C14*: maximum 0.2 per cent;
- *myristic acid*: maximum 0.2 per cent;
- *palmitic acid*: 3.6 per cent to 6.0 per cent;
- *stearic acid*: 1.0 per cent to 5.0 per cent;
- *oleic acid*: 70.0 per cent to 84.0 per cent;
- *linoleic acid*: 7.0 per cent to 23.0 per cent;
- *linolenic acid*: maximum 0.5 per cent;
- *arachidic acid*: maximum 1.0 per cent;
- *eicosenoic acid*: maximum 1.0 per cent;
- *behenic acid*: maximum 1.2 per cent.

Brassicasterol (*2.4.23*): maximum 0.3 per cent in the sterol fraction of the oil.

Water (*2.5.32*): maximum 0.1 per cent, determined on 1.00 g.

STORAGE

In a well-filled, airtight container, protected from light.

LABELLING

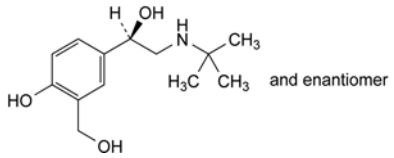
The label states:

- where applicable, that the substance is suitable for use in the manufacture of parenteral preparations;
- the type of oil (type I or type II).

01/2011:0529

SALBUTAMOL

Salbutamolum



$C_{13}H_{21}NO_3$ M_r 239.3

[18559-94-9]

DEFINITION

(1*RS*)-2-[(1,1-Dimethylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanol.

Content: 98.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: sparingly soluble in water, soluble in ethanol (96 per cent).

mp: about 155 °C, with decomposition.

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (*2.2.25*).

Test solution. Dissolve 80.0 mg in a 10 g/L solution of *hydrochloric acid R* and dilute to 100.0 mL with the same acid. Dilute 10.0 mL of the solution to 100.0 mL with a 10 g/L solution of *hydrochloric acid R*.

Spectral range: 230-350 nm.

Absorption maximum: at 276 nm.

Specific absorbance at the absorption maximum: 66 to 75.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *salbutamol CRS*.

C. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 10 mg of the substance to be examined in *methanol R* and dilute to 50 mL with the same solvent.

Reference solution. Dissolve 10 mg of *salbutamol CRS* in *methanol R* and dilute to 50 mL with the same solvent.