Loss on drying (*2.2.32*): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 2 h.

Sulphated ash (*2.4.14*): maximum 0.2 per cent, determined on 1.0 g.

ASSAY

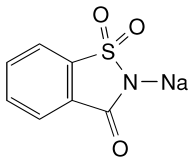
Dissolve 0.500 g in 40 ml of *ethanol (96 per cent) R*. Add 40 ml of *water R*. Titrate with *0.1 M sodium hydroxide*, using a 10 g/l solution of *phenolphthalein R* in *ethanol (96 per cent) R* as indicator. Carry out a blank titration.

1 ml of *0.1 M sodium hydroxide* is equivalent to 18.32 mg of $C_7H_5NO_3S$.

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 *sulphuric 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*-Toluenesulphonamide.** 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 sulphate R* and filter. Wash the filter and the sodium sulphate 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-toluenesulphonamide R* and 20.0 mg of *p-toluenesulphonamide 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*-toluenesulphonamide, *p*-toluenesulphonamide, caffeine.

System suitability:
- *resolution*: minimum 1.5 between the peaks due to *o*-toluenesulphonamide and *p*-toluenesulphonamide 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*-toluenesulphonamide and *p*-toluenesulphonamide.

Limits:

– *o-toluenesulphonamide*: 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-toluenesulphonamide*: 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 *sulphuric 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.

01/2008:2386

SAFFLOWER FLOWER

Carthami flos

DEFINITION

Dried flower of *Carthamus tinctorius* L.

Content: minimum 1.0 per cent of total flavonoids, expressed as hyperoside ($C_{21}H_{20}O_{12}$; M_r 464.4) (dried drug).

IDENTIFICATION

A. The orange-yellow or reddish-orange, tubular, gametalous, actinomorphic florets are separate from the capitulum. Each consists of a long, filiform tube, about 1 cm long divided into 5 equal, narrow, lanceolate lobes, about 0.5 cm long. From the opening of the tube emerges the hollow cylinder formed by the fused yellow anthers, in which the filiform style persists, thickened near the apex.

B. Reduce to a powder (355) (*2.9.12*). The powder is orange-yellow. Examine under a microscope using *chloral hydrate solution R*. The powder shows fragments of the corolla tube with epidermis consisting of elongated, thin-walled polygonal cells; fragments of the lobes of the corolla showing at their apices a large number of small, rounded, very prominent papillae; fragments of parenchyma containing vascular bundles surrounded by secretory canals with reddish-brown contents; fragments of anthers consisting of irregularly shaped cells whose walls show thickenings in characteristic bands; fragments of the style, whose lower part consists of elongated cells and which ends in a stigma, bristling with rather long, conical, confluent papillae; rounded or elliptical triporate pollen grains up to 60 µm in diameter with an echinulate exine; calcium oxalate prisms, either isolated or present in parenchyma cells.

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

Test solution. To 1.0 g of the powdered drug (355) (*2.9.12*) add 10 ml of *methanol R*. Sonicate for 10 min and centrifuge.

Reference solution. Dissolve 1 mg of *rutin R* and 5 mg of *quercetin dihydrate R* in 50 ml of *methanol R*.

Plate: *TLC silica gel plate R* (5-40 µm) [or *TLC silica gel plate R* (2-10 µm)].

Mobile phase: *anhydrous formic acid R, acetic acid R, water R, ethyl acetate R* (11:11:27:100 *V/V/V/V*).

Application: 25 µl as bands of 15 mm [or 10 µl as bands of 8 mm].

Development: over a path of 12 cm [or 7 cm].

Drying: in air.

Detection A: examine in daylight.

Results A: see below the sequence of the zones present in the chromatograms obtained with the reference solution and the test solution. Furthermore, other faint zones may be present in the chromatogram obtained with the test solution.

Top of the plate	
Quercetin: a light yellow zone	
_____	_____
_____	_____
Rutin: a light yellow zone	
	A red zone
	A yellow zone
	A yellow zone
Reference solution	**Test solution**

Detection B: heat the plate at 100 °C for 3 min; spray the plate whilst still hot with a 10 g/l solution of *diphenylboric acid aminoethyl ester R* in *methanol R* and then with a 50 g/l solution of *macrogol 400 R* in *methanol R*; allow the plate to dry in air for about 30 min; examine in ultraviolet light at 365 nm.

Results B: see below the sequence of zones present in the chromatograms obtained with the reference solution and the test solution. Furthermore, other faint zones may be present in the chromatogram obtained with the test solution.