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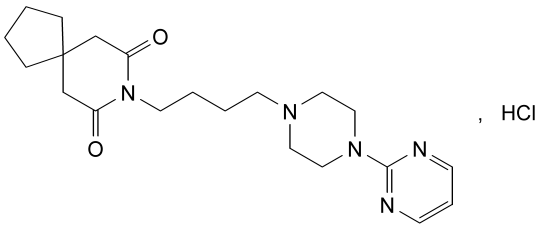
corrected 6.0

BUSPIRONE HYDROCHLORIDE

Buspironi hydrochloridum



, HCl

$C_{21}H_{32}ClN_5O_2$ M_r 422.0
[33386-08-2]

DEFINITION

8-[4-[4-(Pyrimidin-2-yl)piperazin-1-yl]butyl]-8-azaspiro[4.5]decane-7,9-dione hydrochloride.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water and in methanol, practically insoluble in acetone.

It shows polymorphism (*5.9*).

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *buspirone hydrochloride CRS*.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in *methanol R*, evaporate to dryness on a water-bath and record new spectra using the residues.

B. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 25.0 mg of the substance to be examined in mobile phase A and dilute to 25.0 ml with mobile phase A.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with mobile phase A. Dilute 1.0 ml of this solution to 10.0 ml with mobile phase A.

Reference solution (b). Dissolve the contents of a vial of *buspirone for system suitability CRS* (containing impurities E, G, J, L and N) in 2.0 ml of mobile phase A and sonicate for 10 min.

Column:

– *size*: *l* = 0.15 m, Ø = 4.6 mm,
– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm),
– *temperature*: 40 °C.

Mobile phase:

– *mobile phase A*: mix 950 volumes of a solution containing 6.8 g/l of *potassium dihydrogen phosphate R* and 0.93 g/l of *sodium hexanesulphonate monohydrate R*, previously adjusted to pH 3.4 with *phosphoric acid R* and 50 volumes of *acetonitrile R1*;
– *mobile phase B*: mix 250 volumes of a solution containing 3.4 g/l of *potassium dihydrogen phosphate R* and 3.52 g/l of *sodium hexanesulphonate monohydrate R*, previously adjusted to pH 2.2 with *phosphoric acid R* and 750 volumes of *acetonitrile R1*,

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 6	90	10
6 - 34	90 → 42	10 → 58
34 - 45	42	58
45 - 55	42 → 0	58 → 100
55 - 56	0 → 100	100 → 0
56 - 60	100	0
60 - 61	100 → 90	0 → 10

Flow rate: 1 ml/min.

Detection: variable wavelength spectrophotometer capable of operating at 240 nm and at 210 nm.

Injection: 20 µl.

Identification of impurities: use the chromatogram supplied with *buspirone for system suitability CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities E, G, J, L and N.

Relative retention at 240 nm with reference to buspirone (retention time = about 25 min): impurity A = about 0.2; impurity B = about 0.3; impurity C = about 0.6; impurity D = about 0.7; impurity E = about 0.8; impurity F = about 0.9; impurity G = about 1.05; impurity H = about 1.1; impurity I = about 1.2; impurity J = about 1.5.

Relative retention at 210 nm with reference to buspirone (retention time = about 25 min): impurity K = about 0.6; impurity L = about 1.7; impurity M = about 1.8; impurity N = about 1.9.

System suitability: reference solution (b):

– *peak-to-valley ratio at 240 nm*: minimum 5.0, where H_p = height above the baseline of the peak due to impurity G and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to buspirone;
– *resolution at 210 nm*: minimum 4.0 between the peaks due to impurity L and impurity N;
– the chromatograms obtained are similar to the chromatograms supplied with *buspirone for system suitability CRS*.

Limits: spectrophotometer at 240 nm:

– *correction factor*: for the calculation of content, multiply the peak area of impurity J by 2,
– *impurity E*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent),
– *impurity J*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent),
– *any other impurity*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),
– *total*: not more than 4 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.4 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).

Limits: spectrophotometer at 210 nm:

– *impurity K*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),
– *any other impurity eluting with a relative retention greater than 1.6*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent),
– *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 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 1.000 g by drying at 105 °C.

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

ASSAY

Dissolve 0.150 g in 10 ml of *glacial acetic acid R* and add 50 ml of *acetic anhydride 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 21.10 mg of $C_{21}H_{32}ClN_5O_2$.

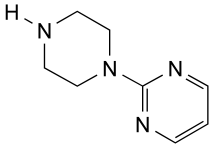
STORAGE

Protected from light.

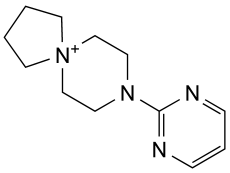
IMPURITIES

Specified impurities: E, J, K.

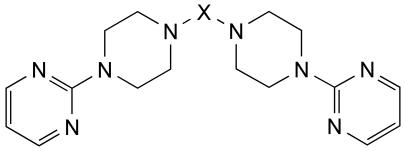
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical 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, F, G, H, I, L, M, N.*



A. 2-(piperazin-1-yl)pyrimidine,

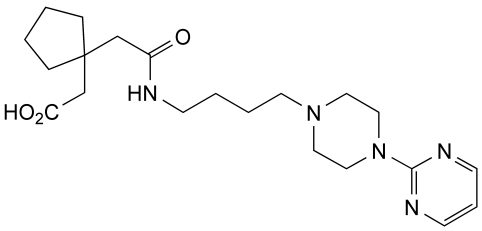


B. 8-(pyrimidin-2-yl)-8-aza-5-azoniaspiro[4.5]decane,

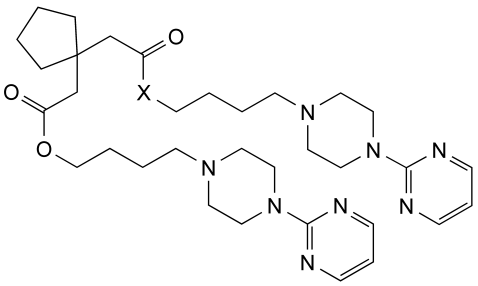


C. X = $[CH_2]_4$: 2,2′-[butane-1,4-diylbis(piperazine-1,4-diyl)]dipyrimidine,

D. X = $[CH_2]_4$-O-$[CH_2]_4$: 2,2′-[oxybis[butane-1,4-diyl(piperazine-1,4-diyl)]]dipyrimidine,

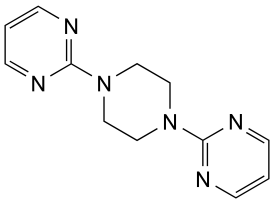


E. [1-[2-oxo-2-[[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl]amino]ethyl]cyclopentyl]acetic acid,

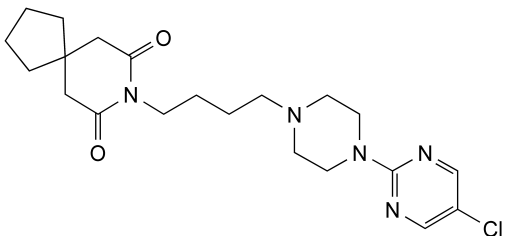


F. X = NH: 4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl [1-[2-oxo-2-[[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl]amino]ethyl]cyclopentyl]acetate,

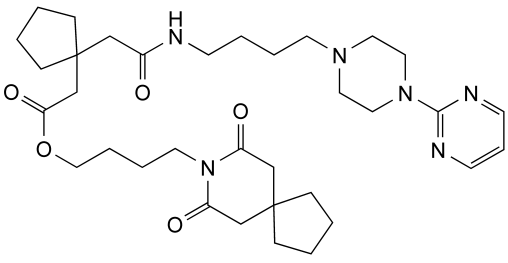
H. X = O: bis[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl] (cyclopentane-1,1-diyl)diacetate,



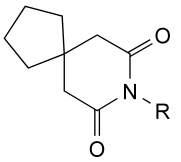
G. 2,2′-(piperazine-1,4-diyl)dipyrimidine,



I. 8-[4-[4-(5-chloropyrimidin-2-yl)piperazin-1-yl]butyl]-8-azaspiro[4.5]decane-7,9-dione,



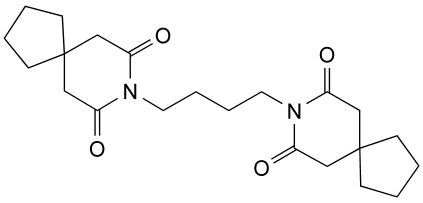
J. 4-(7,9-dioxo-8-azaspiro[4.5]dec-8-yl)butyl [1-[2-oxo-2-[[4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl]amino]ethyl]cyclopentyl]acetate,



K. R = H: 8-azaspiro[4.5]decane-7,9-dione,

L. R = $[CH_2]_4$-Cl: 8-(4-chlorobutyl)-8-azaspiro[4.5]decane-7,9-dione,

M. R = $[CH_2]_4$-Br: 8-(4-bromobutyl)-8-azaspiro[4.5]decane-7,9-dione,



N. 8,8′-(butane-1,4-diyl)bis(8-azaspiro[4.5]decane-7,9-dione).

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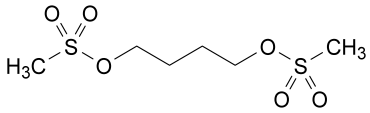
BUSULFAN

Busulfanum



$C_6H_{14}O_6S_2$ M_r 246.3
[55-98-1]

DEFINITION

Butane-1,4-diyl di(methanesulphonate).

Content: 99.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: very slightly soluble in water, freely soluble in acetone and in acetonitrile, very slightly soluble in ethanol (96 per cent).

mp: about 116 °C.

IDENTIFICATION

First identification: A.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *busulfan CRS.*

B. Thin-layer chromatography (*2.2.27*).
Test solution. Dissolve 20 mg of the substance to be examined in 2 ml of *acetone R.*
Reference solution. Dissolve 20 mg of *busulfan CRS* in 2 ml of *acetone R.*
Plate: *TLC silica gel G plate R.*
Mobile phase: *acetone R, toluene R* (50:50 *V/V*).
Application: 5 µl.
Development: over a path of 15 cm.
Drying: in a current of warm air.
Detection: spray with *anisaldehyde solution R* and heat at 120 °C.
Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

C. To 0.1 g add 5 ml of *1 M sodium hydroxide.* Heat until a clear solution is obtained. Allow to cool. To 2 ml of the solution add 0.1 ml of *potassium permanganate solution R.* The colour changes from purple through violet to blue and finally to green. Filter and add 1 ml of *ammoniacal silver nitrate solution R.* A precipitate is formed.

D. To 0.1 g add 0.1 g of *potassium nitrate R* and 0.25 g of *sodium hydroxide R,* mix and heat to fusion. Allow to cool and dissolve the residue in 5 ml of *water R.* Adjust to pH 1-2 using *dilute hydrochloric acid R.* The solution gives reaction (a) of sulphates (*2.3.1*).

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution B_7 (*2.2.2, Method II*).

Dissolve 0.25 g in 20 ml of *acetonitrile R,* dilute to 25 ml with *water R* and examine immediately.

Acidity. Dissolve 0.20 g with heating in 50 ml of *anhydrous ethanol R.* Add 0.1 ml of *methyl red solution R.* Not more than 0.05 ml of *0.1 M sodium hydroxide* is required to change the colour of the indicator.

Loss on drying (*2.2.32*): maximum 2.0 per cent, determined on 1.000 g by drying *in vacuo* at 60 °C.

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

ASSAY

To 0.250 g add 50 ml of *water R.* Shake. Boil under a reflux condenser for 30 min and, if necessary, make up to the initial volume with *water R.* Allow to cool. Using 0.3 ml of *phenolphthalein solution R* as indicator, titrate with *0.1 M sodium hydroxide* until a pink colour is obtained.

1 ml of *0.1 M sodium hydroxide* is equivalent to 12.32 mg of $C_6H_{14}O_6S_2$.

STORAGE

In an airtight container, protected from light.

01/2008:1847
corrected 6.0

BUTCHER'S BROOM

Rusci rhizoma

DEFINITION

Dried, whole or fragmented underground parts of *Ruscus aculeatus* L.

Content: minimum 1.0 per cent of total sapogenins, expressed as ruscogenins [mixture of neoruscogenin ($C_{27}H_{40}O_4$; M_r 428.6) and ruscogenin ($C_{27}H_{42}O_4$; M_r 430.6)] (dried drug).

IDENTIFICATION

A. The rhizome consists of yellowish, branched, articulated, somewhat knotty pieces, cylindrical or subconical, about 5-10 cm long and about 5 mm thick. The surface is marked with thin annulations about 1-3 mm wide, separated from one another; rounded scars of the aerial stems are present on the upper surface. On the lower surface numerous roots, or their scars, occur; the roots