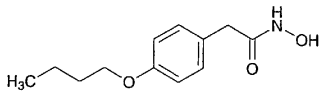
Bufexamac

ブフェキサマク



$C_{12}H_{17}NO_3$: 223.27
2-(4-Butyloxyphenyl)-*N*-hydroxy acetamide [*2438-72-4*]

Bufexamac, when dried, contains not less than 98.0% of $C_{12}H_{17}NO_3$.

Description Bufexamac occurs as white to pale yellowish white crystals or crystalline powder. It has a faint, characteristic odor, and is tasteless.

It is freely soluble in *N,N*-dimethylformamide, sparingly soluble in methanol and in ethanol (95), and practically insoluble in water and in diethyl ether.

Melting point: about 162°C (with decomposition).

Identification (1) To 5 mL of a solution of Bufexamac in methanol (1 in 5000) add 1 drop of iron (III) chloride-methanol TS, and shake: a dark red color develops.

(2) Determine the absorption spectrum of a solution of Bufexamac in ethanol (95) (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(3) Determine the infrared absorption spectrum of Bufexamac as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

Purity (1) Clarity and color of solution—Dissolve 0.20 g of Bufexamac in 20 mL of ethanol (95): the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g of Bufexamac according to Method 4, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(3) Arsenic—Prepare the test solution with 1.0 g of Bufexamac according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(4) Related substances—Dissolve 0.20 g of Bufexamac in 10 mL of methanol, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add methanol to make exactly 100 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Use a plate of silica gel with fluorescent indicator for thin-layer chromatography, moisten the surface of the plate evenly by spraying with 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS, and dry at 110°C for about 30 minutes. Spot 15 μL each of the sample solution and the standard solution on the plate. Develop the plate with a mixture of chloroform, cyclohexane, methanol and acetic acid (100) (6:4:1:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots other than the principal spot from the sample solution are not more intense than the spot from the standard solution.

Loss on drying Not more than 0.5% (1 g, 105°C, 4 hours).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.2 g of Bufexamac, previously dried, dissolve in 40 mL of *N,N*-dimethylformamide, and titrate with 0.1 mol/L tetramethylammonium hydroxide-methanol VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L tetramethylammonium hydroxide-methanol VS
= 22.327 mg of $C_{12}H_{17}NO_3$

Containers and storage Containers—Tight containers.

Bufexamac Cream

ブフェキサマク乳剤性軟膏

Bufexamac Cream contains not less than 90% and not more than 110% of the labeled amount of bufexamac ($C_{12}H_{17}NO_3$: 223.27).

Method of preparation Prepared as directed under Ointments, with Bufexamac.

Description Bufexamac Cream is white.
pH: 4.0 - 6.0

Identification To a quantity of Bufexamac Cream, equivalent to 0.05 g of Bufexamac according to the labeled amount, add 10 mL of tetrahydrofuran, shake well, centrifuge, and use the supernatant liquid as the sample solution. Separately, dissolve 0.05 g of bufexamac for assay in 10 mL of methanol, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Use a plate of silica gel for thin-layer chromatography, moisten the surface of the plate evenly by spraying with 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS, and dry the plate at 110°C for about 30 minutes. Spot 5 μL each of the sample solution and the standard solution on the plate. Develop the plate with a mixture of pentane, ethyl acetate and acetic acid (100) (7:4:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly iron (III) chloride TS on the plate: the spot from the sample solution and that from the standard solution show a red-brown color and the same *Rf* value.

Assay Weigh accurately a quantity of Bufexamac Cream, equivalent to about 0.05 g of bufexamac ($C_{12}H_{17}NO_3$), dissolve in 40 mL of methanol, and add methanol to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 5 mL of the internal standard solution and add the mobile phase to make 100 mL, filter, and use the filtrate as the sample solution. Separately, weigh accurately about 0.05 g of bufexamac for assay, previously dried at 105°C for 4 hours, and dissolve in methanol to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 5 mL of the internal standard solution, add the mobile phase to make 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as

directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of bufexamac to that of the internal standard, respectively.

$$\text{Amount (mg) of bufexamac } (C_{12}H_{17}NO_3) = \text{amount (mg) of bufexamac for assay} \times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of diphenylimidazole in methanol (1 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 275 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

Mobile phase: Dissolve 2.5 g of sodium 1-octane sulfonate and 0.6 g of disodium dihydrogen ethylenediamine tetraacetate dihydrate in 850 mL of water, and add 400 mL of methanol, 400 mL of acetonitrile and 8 mL of acetic acid (100).

Flow rate: Adjust the flow rate so that the retention time of bufexamac is about 6 minutes.

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, bufexamac and the internal standard are eluted in this order with the resolution between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of bufexamac to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Tight containers.

Bufexamac Ointment

ブフェキサマク軟膏

Bufexamac Ointment contains not less than 90% and not more than 110% of the labeled amount of bufexamac ($C_{12}H_{17}NO_3$: 223.27).

Method of preparation Prepare as directed under Ointments, with Bufexamac.

Identification To a quantity of Bufexamac Ointment, equivalent to 0.05 g of Bufexamac according to the labeled amount, add 5 mL of tetrahydrofuran, shake well, add 5 mL of ethanol (99.5), shake, centrifuge, and use the supernatant liquid as the sample solution. Separately, dissolve 0.05 g of bufexamac for assay in 10 mL of methanol, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Use a plate of silica gel for thin-layer chromatography, moisten the surface of the plate evenly by spraying with 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS, and dry the plate at 110°C for about 30 minutes. Spot 5 μL each of the sample solution and the standard solution on the plate. Develop the plate with a mixture of pentane, ethyl acetate and acetic acid (100) (7:4:1) to a distance of about 10 cm, and air-dry the plate. Spray evenly iron (III) chloride TS on the plate: the spot from the sample solution and that from the standard solution show a red-brown color and the same *Rf* value.

Assay Weigh accurately a quantity of Bufexamac Ointment, equivalent to about 0.05 g of bufexamac ($C_{12}H_{17}NO_3$), add 40 mL of tetrahydrofuran, warm to 40°C, dissolve by shaking, cool, and add tetrahydrofuran to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 5 mL of the internal standard solution and the mobile phase to make 100 mL, and filter, if necessary, through a membrane filter of 0.45-μm porosity. Discard the first 20 mL of the filtrate, and use the subsequent filtrate as the sample solution. Separately, weigh accurately about 0.05 g of bufexamac for assay, previously dried at 105°C for 4 hours, and dissolve in tetrahydrofuran to make exactly 50 mL. Pipet 10 mL of this solution, add exactly 5 mL of the internal standard solution and the mobile phase to make 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of bufexamac to that of the internal standard, respectively.

$$\text{Amount (mg) of bufexamac } (C_{12}H_{17}NO_3) = \text{amount (mg) of bufexamac for assay} \times \frac{Q_T}{Q_S}$$

Internal standard solution—A solution of diphenylimidazole in methanol (1 in 5000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 275 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 25°C.

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Flow rate: Adjust the flow rate so that the retention time of bufexamac is about 6 minutes.

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, bufexamac and the internal standard are eluted in this order with the resolution between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of bufexamac to that of the internal standard is not more than 1.0%.