(2) Weigh a portion of powdered Aspirin Tablets, equivalent to 0.5 g of Aspirin according to the labeled amount, extract with two 10-mL portions of warm ethanol (95), and filter the combined extracts. Evaporate the filtrate to dryness, and boil the residue with 10 mL of sodium carbonate TS for 5 minutes. Proceed as directed in the Identification (2) under Aspirin.

Purity Salicylic acid—Take a portion of the powdered Aspirin Tablets, equivalent to 1.0 g of Aspirin according to the labeled amount, shake with 15 mL of ethanol (95) for 5 minutes, filter, discard the first 5 mL of the filtrate, and add 1.0 mL of the subsequent filtrate to a solution which is prepared by transferring 1 mL of freshly prepared dilute ammonium iron (III) sulfate TS to a Nessler tube and diluting with water to make 50 mL. Proceed as directed in the Purity (2) under Aspirin.

Assay Weigh accurately and powder not less than 20 Aspirin Tablets. Weigh accurately a portion of the powder, equivalent to about 1.5 g of aspirin ($C_9H_8O_4$), add exactly 50 mL of 0.5 mol/L sodium hydroxide VS, and proceed as directed in the Assay under Aspirin.

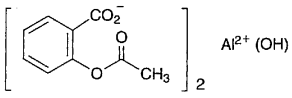
Each mL of 0.5 mol/L sodium hydroxide VS
= 45.04 mg of $C_9H_8O_4$

Containers and storage Containers—Well-closed containers.

Aspirin Aluminum

Aluminum Acetylsalicylate

アスピリンアルミニウム



$C_{18}H_{15}AlO_9$: 402.29
Bis(2-acetoxybenzoato)hydroxoaluminium [*23413-80-1*]

Aspirin Aluminum contains not less than 83.0% and not more than 90.0% of aspirin ($C_9H_8O_4$: 180.16), and not less than 6.0% and not more than 7.0% of aluminum (Al: 26.98), calculated on the anhydrous basis.

Description Aspirin Aluminum occurs as a white, crystalline powder. It is odorless or has a slight, acetic odor.

It is practically insoluble in water, in methanol, in ethanol (95) and in diethyl ether.

It dissolves, with decomposition, in sodium hydroxide TS and in sodium carbonate TS.

Identification (1) Dissolve 0.1 g of Aspirin Aluminum in 10 mL of sodium hydroxide TS by heating, if necessary. Neutralize 2 mL of the solution with hydrochloric acid, and add 1 to 2 drops of iron (III) chloride TS: a red-purple color develops.

(2) Determine the absorption spectrum of the sample solution obtained in the Assay (1) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 277 nm and 279 nm.

(3) Place 2 g of Aspirin Aluminum in a platinum crucible, and ignite until charred. To the residue add 1 g of anhydrous sodium carbonate, and ignite for 20 minutes. After cooling, to the residue add 15 mL of dilute hydrochloric acid, shake, and filter: the filtrate responds to the Qualitative Tests for aluminum salt.

Purity (1) Salicylate—Using A_{T2} and A_{S2} obtained in the Assay (1), calculate the amount of salicylate [as salicylic acid ($C_7H_6O_3$: 138.12)] by the following equation: salicylate content is not more than 7.5%, calculated on the anhydrous basis.

$$\text{Amount (mg) of salicylic acid } (C_7H_6O_3) = \text{amount (mg) of salicylic acid for assay} \times \frac{A_{T2}}{A_{S2}} \times \frac{1}{4}$$

(2) Heavy metals—Place 2.0 g of Aspirin Aluminum in a porcelain crucible, cover the crucible loosely, and ignite at a low temperature until charred. After cooling, add 2 mL of nitric acid and 1 mL of sulfuric acid to the content of the crucible, heat gently the crucible until white fumes are evolved, and continue the heating until white fumes are no longer evolved, then ignite between 500°C and 600°C until the carbon is incinerated. When the incineration is not completed, add 2 mL of nitric acid and 1 mL of sulfuric acid, and heat gently in the same manner, then ignite between 500°C and 600°C to incinerate completely. After cooling, add 2 mL of hydrochloric acid, and proceed as directed in Method 2, and perform the test. Prepare the control solution by using the same quantities of the same reagents as directed for the preparation of the test solution, and add 2.0 mL of Standard Lead Solution and water to make 50 mL (not more than 10 ppm).

(3) Arsenic—Dissolve 1.0 g of Aspirin Aluminum in 15 mL of sodium hydroxide TS. To this solution add 1 drop of phenolphthalein TS, and with stirring, add dropwise hydrochloric acid until the red color of the solution disappears. Then add 2 mL of hydrochloric acid, cool with occasional shaking for 10 minutes, and filter with a glass filter (G3). Wash the residue with two 5 mL portions of 1 mol/L hydrochloric acid TS, and combine the filtrate and the washings. Use this solution as the test solution, and perform the test using Apparatus B (not more than 2 ppm).

Water Not more than 4.0% (0.15 g, direct titration).

Assay (1) Aspirin—Weigh accurately about 0.1 g of Aspirin Aluminum, add 40 mL of sodium fluoride TS, and shake for 5 minutes. Allow the solution to stand for 10 minutes with frequent shaking. Extract the solution with six 20-mL portions of chloroform. Combine all chloroform extracts, and add chloroform to make exactly 200 mL. Measure exactly 10 mL of this solution, add chloroform to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.09 g of salicylic acid for assay, previously dried in a desiccator (silica gel) for 3 hours, and dissolve in chloroform to make exactly 200 mL. Measure exactly 5 mL of this solution, add chloroform to make exactly 200 mL, and use this solution as the standard solution (1). Then weigh accurately about 0.09 g of aspirin for assay, previously dried in a desiccator (silica gel) for 5 hours, and dissolve in chloroform to make exactly 200 mL. Measure exactly 10 mL of this solution, add chloroform to

make exactly 100 mL, and use this solution as the standard solution (2). Perform the test with these solutions as directed under the Ultraviolet-visible Spectrophotometry. Determine the absorbances, A_{T1} and A_{S1}, of the sample solution and the standard solution (1) at 278 nm, and absorbances, A_{T2} and A_{S2}, of these solution, at 308 nm, respectively. Then determine the absorbance A_{S3} of the standard solution (2) at 278 nm.

$$\text{Amount (mg) of aspirin } (C_9H_8O_4) = \text{amount (mg) of aspirin for assay} \times \left[\frac{A_{T1} - \frac{A_{T2} \times A_{S1}}{A_{S2}}}{A_{S3}}\right]$$

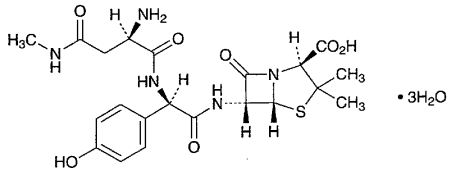
(2) Aluminum—Weigh accurately about 0.4 g of Aspirin Aluminum, and dissolve in 10 mL of sodium hydroxide TS. Add dropwise 1 mol/L hydrochloric acid TS to adjust the solution to a pH of about 1, add 20 mL of acetic acid-ammonium acetate buffer solution, pH 3.0, and 0.5 mL of Cu-PAN TS, and heat. While boiling, titrate with 0.05 mol/L disodium dihydrogen ethylenediamine tetraacetate VS until the color of the solution changes from red to yellow and persists for 1 minute. Perform a blank determination, and make any necessary correction.

Each mL of 0.05 mol/L disodium dihydrogen ethylenediamine tetraacetate VS
= 1.3491 mg of Al

Containers and storage Containers—Well-closed containers.

Aspoxicillin

アスポキシシリン



$C_{21}H_{27}N_5O_7S.3H_2O$: 547.58
(2*S*,5*R*,6*R*)-6-[(2*R*)-2-[(2*R*)-2-Amino-3-methylcarbamoylpropanoylamino]-2-(4-hydroxyphenyl)acetylamino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid trihydrate
[*63358-49-6*, anhydride]

Aspoxicillin contains not less than 950 μg (potency) per mg, calculated on the anhydrous basis. The potency of Aspoxicillin is expressed as mass (potency) of aspoxicillin ($C_{21}H_{27}N_5O_7S$: 493.53).

Description Aspoxicillin occurs as a white, crystals or crystalline powder.

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

Identification **(1)** Determine the absorption spectrum of a solution of Aspoxicillin (1 in 4000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum or the spectrum of Aspoxicillin Reference Standard: both spectra exhibit similar intensities of absorption at the same wavelength.

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

Optical rotation $[\alpha]_D^{20}$: +170 – +185° (0.2 g calculated on the anhydrous bases, water, 20 mL, 100 mm).

pH Dissolve 0.1 g of Aspoxicillin in 50 mL of water: the pH of the solution is between 4.2 and 5.2.

Purity **(1)** Clarity and color of solution—Dissolve 1.0 g of Aspoxicillin in 50 mL of water: the solution is clear and colorless.

(2) Heavy metals—Proceed with 2.0 g of Aspoxicillin according to Method 2, 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 2.0 g of Aspoxicillin according to Method 5, and perform the test using Apparatus B (not more than 1 ppm).

(4) Related substances—Dissolve 0.05 g of Aspoxicillin in 10 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 10 μL each of these solutions as directed under the Liquid Chromatography according to the following conditions, and calculate the areas of each peak by the automatic integration method: the area of each peak other than aspoxicillin from the sample solution is not more than 3/10 of the peak area of aspoxicillin from the standard solution, and the total of peak areas other than aspoxicillin from the sample solution is not more than the peak area of aspoxicillin from the standard solution.

Operating conditions—

Detector, column, column temperature, mobile phase, and flow rate: Proceed as directed in the operating conditions in the Assay.

Time span of measurement: About 6 times as long as the retention time of aspoxicillin.

System suitability—

Test for required detection: Pipet 2 mL of the standard solution, add the mobile phase to make exactly 10 mL. Confirm that the peak area of aspoxicillin obtained from 10 μL of this solution is equivalent to 15 to 25% of that of aspoxicillin obtained from 10 μL of the standard solution.

System performance: Proceed as directed in the system suitability in the Assay.

System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of aspoxicillin is not more than 5%.

Water Not less than 9.5% and not more than 13.0% (0.2 g, volumetric titration, direct titration).

Assay Weigh accurately an amount of Aspoxicillin and Aspoxicillin Reference Standard, equivalent to about 0.1 g