» Aspartic Acid contains not less than 98.5 percent and not more than 101.5 percent of $C_4H_7NO_4$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers, protected from light.

USP Reference standards ⟨11⟩—*USP Aspartic Acid RS.*

Identification, *Infrared Absorption* ⟨197K⟩.

Specific rotation ⟨781S⟩: between +24.0° and +26.0°, at 20°.

Test solution: 80 mg per mL, in 6 N hydrochloric acid.

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Chloride ⟨221⟩—Dissolve 0.7 g in 10 mL of diluted nitric acid, and dilute with water to make 15 mL: the solution shows no more chloride than corresponds to 0.20 mL of 0.020 N hydrochloric acid (0.02%).

Sulfate ⟨221⟩—Dissolve 0.8 g in 4 mL of hydrochloric acid, and dilute with water to make 15 mL: the solution shows no more sulfate than corresponds to 0.25 mL of 0.020 N sulfuric acid (0.03%).

Iron ⟨241⟩: 0.001%.

Heavy metals, *Method II* ⟨231⟩: 0.001%.

Chromatographic purity—

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture.

System suitability solution—Dissolve 10 mg each of USP Aspartic Acid RS and glutamic acid, each accurately weighed, in 2 mL of ammonia TS, dilute with water to 25.0 mL, and mix.

Test solution—Transfer 0.1 g of Aspartic Acid to a 10-mL volumetric flask, dissolve in 2 mL of 17% ammonia solution (prepared by diluting ammonium hydroxide, 6 in 10), dilute with water to volume, and mix.

Standard solution—Transfer 5 mg of USP Aspartic Acid RS to a 100-mL volumetric flask, dissolve in 2 mL of 17% ammonia solution (prepared by diluting ammonium hydroxide, 6 in 10), dilute with water to volume, and mix.

Application volume: 5 µL.

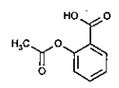
Developing solvent system: a mixture of butyl alcohol, glacial acetic acid, and water (6 : 2 : 2).

Spray reagent—Dissolve 0.2 g of ninhydrin in 100 mL of a mixture of butyl alcohol and 2 N acetic acid (95 : 5).

Procedure—Proceed as directed for *Thin-Layer Chromatography* under *Chromatography* ⟨621⟩, except to dry the plate at 80° for 30 minutes, spray with *Spray reagent,* and heat at 80° for 30 minutes. Examine the plate under white light. The chromatogram obtained from the *System suitability solution* exhibits two clearly separated spots, and no secondary spot in the chromatogram of the *Test solution* is larger or more intense than the principal spot in the chromatogram of the *Standard solution:* not more than 0.5% of any individual impurity is found; and not more than 2.0% of total impurities is found.

Assay—Transfer about 0.1 g of Aspartic Acid, accurately weighed, to a 125-mL flask, and dissolve in 50 mL of carbon dioxide-free water, heating slightly if necessary. Cool, add 0.1 mL of bromothymol blue TS, and titrate with 0.1 N sodium hydroxide VS until the color changes from yellow to blue. Perform a blank determination, and make any necessary correction (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N sodium hydroxide is equivalent to 13.31 mg of $C_4H_7NO_4$.

Aspirin



$C_9H_8O_4$ 180.16
Benzoic acid, 2-(acetyloxy)-.
Salicylic acid acetate [*50-78-2*].

» Aspirin contains not less than 99.5 percent and not more than 100.5 percent of $C_9H_8O_4$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Aspirin RS.*

Identification—

A: Heat it with water for several minutes, cool, and add 1 or 2 drops of ferric chloride TS: a violet-red color is produced.

B: *Infrared Absorption* ⟨197K⟩.

Loss on drying ⟨731⟩—Dry it over silica gel for 5 hours: it loses not more than 0.5% of its weight.

Readily carbonizable substances ⟨271⟩—Dissolve 500 mg in 5 mL of sulfuric acid TS: the solution has no more color than *Matching Fluid Q.*

Residue on ignition ⟨281⟩: not more than 0.05%.

Substances insoluble in sodium carbonate TS—A solution of 500 mg in 10 mL of warm sodium carbonate TS is clear.

Chloride ⟨221⟩—Boil 1.5 g with 75 mL of water for 5 minutes, cool, add sufficient water to restore the original volume, and filter. A 25-mL portion of the filtrate shows no more chloride than corresponds to 0.10 mL of 0.020 N hydrochloric acid (0.014%).

Sulfate —Dissolve 6.0 g in 37 mL of acetone, and add 3 mL of water. Titrate potentiometrically with 0.02 M lead perchlorate, prepared by dissolving 9.20 g of lead perchlorate in water to make 1000 mL of solution, using a pH meter capable of a minimum reproducibility of ±0.1 mV (see *pH* ⟨791⟩) and equipped with an electrode system consisting of a lead-specific electrode and a silver–silver chloride reference glass-sleeved electrode containing a solution of tetraethylammonium perchlorate in glacial acetic acid (1 in 44) (see *Titrimetry* ⟨541⟩): not more than 1.25 mL of 0.02 M lead perchlorate is consumed (0.04%). [NOTE—After use, rinse the lead-specific electrode with water, drain the reference electrode, flush with water, rinse with methanol, and allow to dry.]

Heavy metals—Dissolve 2 g in 25 mL of acetone, and add 1 mL of water. Add 1.2 mL of thioacetamide–glycerin base TS and 2 mL of *pH 3.5 Acetate Buffer* (see *Heavy Metals* ⟨231⟩), and allow to stand for 5 minutes: any color produced is not darker than that of a control made with 25 mL of acetone and 2 mL of *Standard Lead Solution* (see *Heavy Metals* ⟨231⟩), treated in the same manner. The limit is 10 µg per g.

Limit of free salicylic acid—Dissolve 2.5 g in sufficient alcohol to make 25.0 mL. To each of two matched color-comparison tubes add 48 mL of water and 1 mL of a freshly prepared, diluted ferric ammonium sulfate solution (prepared by adding 1 mL of 1 N hydrochloric acid to 2 mL of ferric ammonium sulfate TS and diluting with water to 100 mL). Into one tube pipet 1 mL of a standard solution of salicylic acid in water, containing 0.10 mg of salicylic acid per mL. Into the second tube pipet 1 mL of the 1 in 10 solution of Aspirin. Mix the contents of each tube: after 30 seconds, the color in the second tube is not more intense than that in the tube containing the salicylic acid (0.1%).

Assay—Place about 1.5 g of Aspirin, accurately weighed, in a flask, add 50.0 mL of 0.5 N sodium hydroxide VS, and boil the mixture gently for 10 minutes. Add phenolphthalein TS, and titrate the excess sodium hydroxide with 0.5 N sulfuric acid VS. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.5 N sodium hydroxide is equivalent to 45.04 mg of $C_9H_8O_4$.

Aspirin Boluses

» Aspirin Boluses contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of aspirin ($C_9H_8O_4$).

Packaging and storage—Preserve in tight containers.

Labeling—Label Boluses to indicate that they are for veterinary use only.

USP Reference standards ⟨11⟩—*USP Aspirin RS. USP Salicylic Acid RS.*

Identification—

A: Crush 1 Bolus, boil a portion of the powder, equivalent to about 300 mg of aspirin, with 50 mL of water, cool, and add a drop of ferric chloride TS: a violet-red color is produced.

B: The retention time of the aspirin peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩—

Medium: 0.5 M phosphate buffer, pH 7.4; 900 mL.

Apparatus 2: 75 rpm.

Time: 45 minutes.

Diluting solution—Prepare a mixture of acetonitrile and formic acid (99 : 1).

Procedure—Determine the amount of aspirin ($C_9H_8O_4$) dissolved by employing UV absorption at the wavelength of the isosbestic point of aspirin and salicylic acid at 265 ± 2 nm on filtered portions of the solution under test, suitably diluted with *Diluting solution,* if necessary, in comparison with a Standard solution having a known concentration of USP Aspirin RS in the same *Medium.* [NOTE—Prepare the Standard solution at the time of use.]

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_9H_8O_4$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Limit of salicylic acid—Using the chromatograms of the *Standard preparation* and the *Assay preparation,* obtained as directed in the *Assay,* calculate the percentage of salicylic acid ($C_7H_6O_3$) in the portion of Boluses taken by the formula:

$$100{,}000(C / W_A)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Salicylic Acid RS in the *Standard preparation;* W_A is the quantity, in mg, of aspirin ($C_9H_8O_4$) in the portion of Boluses taken, as determined in the *Assay;* and r_U and r_S are the salicylic acid peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively: not more than 0.3% is found.

Assay—

Mobile phase—Dissolve 2 g of sodium 1-heptanesulfonate in a mixture of 850 mL of water and 150 mL of acetonitrile, and adjust with glacial acetic acid to a pH of 3.4. Make any necessary adjustments (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluting solution—Prepare a mixture of acetonitrile and formic acid (99 : 1).

Standard preparation—Prepare a solution in *Diluting solution* having known concentrations of about 0.4 mg of USP Aspirin RS and 0.01 mg of USP Salicylic Acid RS per mL.

Assay preparation—Weigh and finely powder not fewer than 10 Boluses. Transfer an accurately weighed portion of the powder, equivalent to about 400 mg of aspirin, to a 100-mL volumetric flask, dilute with *Diluting solution* to volume, and stir by mechanical means for about 15 minutes. Pass a portion of this solution through a filter having a 0.5-µm or finer porosity, and use the filtrate as the *Assay preparation.*

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.6 for salicylic acid and 1.0 for aspirin, and the relative standard deviation of the aspirin peak response for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of aspirin ($C_9H_8O_4$) in the portion of Boluses taken by the formula:

$$1000C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Aspirin RS in the *Standard preparation;* and r_U and r_S are the aspirin peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Aspirin Capsules

» Aspirin Capsules contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of aspirin ($C_9H_8O_4$).

NOTE—Capsules that are enteric-coated or the contents of which are enteric-coated meet the requirements for *Aspirin Delayed-Release Capsules.*

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Aspirin RS.*

Identification—

A: Heat about 100 mg of the Capsule contents with 10 mL of water for several minutes, cool, and add 1 drop of ferric chloride TS: a violet-red color is produced.

B: Shake a quantity of the contents of Capsules, equivalent to about 500 mg of aspirin, with 10 mL of alcohol for several minutes. Centrifuge the mixture. Pour off the clear supernatant and evaporate it to dryness. Dry the residue in vacuum at 60° for 1 hour: the residue responds to *Identification* test *B* under *Aspirin.*

Dissolution ⟨711⟩—

Medium: 0.05 M acetate buffer, prepared by mixing 2.99 g of sodium acetate trihydrate and 1.66 mL of glacial acetic acid with water to obtain 1000 mL of solution having a pH of 4.50 ± 0.05; 500 mL.

Apparatus 1: 100 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_9H_8O_4$ dissolved from UV absorbances at the wavelength of the isosbestic point of aspirin and salicylic acid at 265 ± 2 nm of filtered portions of the solution under test, suitably diluted with *Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Aspirin RS in the same *Medium.* [NOTE—Prepare the Standard solution at the time of use. An amount of alcohol not to exceed 1% of the total volume of the Standard solution may be used to bring the Reference Standard into solution prior to dilution with *Medium.*]

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_9H_8O_4$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Limit of free salicylic acid—

Ferric chloride-urea reagent—Dissolve by swirling, without the aid of heat, 60 g of urea in a mixture of 8 mL of ferric chloride solution (6 in 10) and 42 mL of 0.05 N hydrochloric acid. Adjust the resulting solution, if necessary, with 6 N hydrochloric acid to a pH of 3.2.

Standard preparation—Transfer 75.0 mg of salicylic acid, previously dried over silica gel for 3 hours and accurately weighed, to a