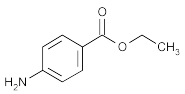
Assay—Transfer 50.0 mL of Tincture to a 150-mL beaker, and add, with continuous stirring, 10 mL of sodium tetraphenylboron solution (1 in 40). Cover, and allow to stand for 16 hours. Decant the supernatant into a tared sintered-glass crucible, applying vacuum filtration. Suspend the precipitate in 20 mL of water, and transfer the precipitate to the crucible, washing well with water. Dry the precipitate and the crucible at 105 ° for 1 hour, cool, and weigh. The weight of the precipitate so obtained, multiplied by 0.6122, represents its equivalent of $C_{27}H_{42}ClNO_2$.

Benzocaine



$C_9H_{11}NO_2$ 165.19
Benzoic acid, 4-amino-, ethyl ester.
Ethyl *p*-aminobenzoate [94-09-7].

» Benzocaine, dried over phosphorus pentoxide for 3 hours, contains not less than 98.0 per cent and not more than 102.0 per cent of $C_9H_{11}NO_2$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩**—**
USP Benzocaine RS

Identification—

A: *Infrared Absorption* ⟨197K⟩: previously dried over phosphorus pentoxide for 3 hours.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 5 µg per mL.

Medium: chloroform.

Absorptivities at 278 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: Dissolve about 20 mg in 10 mL of water with the aid of a few drops of 3 N hydrochloric acid, and add 5 drops of a solution of sodium nitrite (1 in 10), followed by 2 mL of a solution of 100 mg of 2-naphthol in 5 mL of 1 N sodium hydroxide: an orange-red precipitate is formed.

Melting range, *Class I* ⟨741⟩**:** between 88° and 92°, but the range between beginning and end of melting does not exceed 2°.

Reaction—Dissolve 1.0 g in 10 mL of neutralized alcohol: a clear solution results. Dilute this solution with 10 mL of water, and add 2 drops of phenolphthalein TS and 1 drop of 0.10 N sodium hydroxide: a red color is produced.

Loss on drying ⟨731⟩**—**Dry it over phosphorus pentoxide for 3 hours: it loses not more than 1.0% of its weight.

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

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

Chloride—To a solution of 200 mg in 5 mL of alcohol, previously acidified with a few drops of diluted nitric acid, add a few drops of silver nitrate TS: no turbidity is produced immediately.

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

Ordinary impurities ⟨466⟩**—**

Test solution: dehydrated alcohol.

Standard solution: dehydrated alcohol.

Application volume: 10 µL.

Eluant: chloroform containing about 0.75% of dehydrated alcohol as a preservative, in a nonequilibrated chamber.

Visualization: 1.

*Limit—*The total of any ordinary impurities observed does not exceed 1%.

Assay—

*Aqueous solution—*To 980 mL of water, add 20 mL of acetic acid and 1 mL of triethylamine, and mix well. The pH should be between 2.95 and 3.0; adjust as needed.

*Mobile phase—*Prepare a filtered and degassed mixture of *Aqueous solution* and methanol (60:40).

*Standard preparation—*Dissolve an accurately weighed quantity of USP Benzocaine RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.024 mg per mL.

*Assay preparation—*Transfer about 24 mg of Benzocaine, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Dilute 10 mL of this solution with *Mobile phase* to 100 mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 285-nm detector and a 2.0-mm × 15-cm column that contains 5- µm packing L11. The flow rate is about 0.2 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor of the benzocaine peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure—*Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the benzocaine peaks. Calculate the quantity, in mg, of $C_9H_{11}NO_2$ in the portion of Benzocaine taken by the formula:

$$1000C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Benzocaine RS in the *Standard preparation;* r_U and r_S are the peak responses obtained from the *Assay preparation* and *Standard preparation,* respectively; and 1000 is the dilution factor for the *Assay preparation.*

Benzocaine Topical Aerosol

» Benzocaine Topical Aerosol is a solution of Benzocaine in a pressurized container. It contains not less than 90.0 per cent and not more than 110.0 percent of the labeled amount of $C_9H_{11}NO_2$.

Packaging and storage—Preserve in pressurized containers, and avoid exposure to excessive heat.

Identification—Spray a portion of Topical Aerosol into a beaker, and heat on a steam bath for a few minutes to expel residual propellant. A portion of this solution, equivalent to about 5 mg of benzocaine, responds to the *Identification* test under *Benzocaine Topical Solution.*

Other requirements—It meets the requirements for *Pressure Test, Minimum Fill,* and *Leakage Test* under *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩.

Assay—Spray a portion of Topical Aerosol into a beaker, and heat on a steam bath for a few minutes to expel residual propellant. Cool, and transfer an accurately weighed portion of the solution, equivalent to about 200 mg of benzocaine, to a 250-mL beaker. Add 50 mL of water and 5 mL of hydrochloric acid, and stir. Cool the solution in an ice bath to about 10 °, and titrate slowly with 0.1 M sodium nitrite VS, determining the endpoint potentiometrically, using a calomel-platinum electrode system. Perform a blank determination, and make any necessary