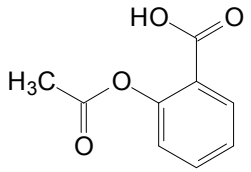
课外阅读一　阿司匹林及其片剂的质量标准（USP）

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 500mg 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 500mg in 10 mL of warm sodium carbonate TS is clear.

Chloride <221>－Boil 1.5g 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 6.0g 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 1000mL of solution, using a pH meter capable of a minimum reproducibility of ±0.1 mV (see pH <791>) 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 1.25mL 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 10μg per g.

Limit of free salicylic acid—Dissolve 2.5g 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%).

Organic volatile impurities, *Method IV* <467>: meets the requirements.

Assay—Place about 1.5g 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 Tablets

>> Aspirin Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_9H_8O_4$. Tablets of larger than 81-mg size contain no sweeteners or other flavors.

N_{OTE}-Tablets that are enteric-coated meet the requirements for *Aspirin Delayed-release Tablets*.

Packaging and storage-Preserve in tight containers. Preserve flavored or sweetened Tablets of 81-mg size or smaller in containers holding not more than 36 Tablets each.

USP Reference standards <11>-*USP Aspirin RS. USP Salicylic Acid RS.*

Identification-

A: Crush 1 Tablet, boil it with 50 mL of water for 5 minutes, cool, and add 1 or 2 drops of ferric chloride TS: a violet-red color is produced.

B: Infrared absorption <197K>-Prepare the test specimen as follows. Shake a quantity of finely powdered Tablets, equivalent to about 500 mg of aspirin, with 10 mL of alcohol for several minutes. Centrifuge the mixture. Pour off the clear supernatant liquid, and evaporate it to dryness. Dry the residue in vacuum at 60℃ for 1 hour.

Dissolution <711>-

Medium: 0.5 *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 1000mL of solution having a pH of 4.50±0.05; 500 mL.

Apparatus 1 : 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_9H_8O_4$ dissolved from ultraviolet absorbances at the wavelength of the isosbestic point of aspirin and salicylic acid at 265±2nm of filtered portions of the solution under test, suitably diluted with *Dissolution 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 *Dissolution Medium*.]

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

Uniformity of dosage units <905>: meet the requirements

Limit of free salicylic acid-

Mobile phase and *Diluting Solution*-Prepare as directed in the *Assay.*

Standard solution-Dissolve an accurately weighed quantity of USP Salicylic Acid RS in the *Standard preparation* prepared as directed in the *Assay*, to obtain a solution having a known concentration of about 0.015 mg of salicylic acid per mL.

Test preparation-Use the Stock solution prepared as directed for *Assay preparation* in the Assay.

Chromatographic system-Use the *Chromatographic system* described in the *Assay*. Chromatograph the *Standard solution*, and record the peak responses as directed under *Procedure* in the *Assay*. The relative standard deviation of the salicylic acid peak responses is not more than 4.0%. In a suitable chromatogram, the resolution, R, between salicylic acid and aspirin is not less than 2.0.

Procedure-Proceed as directed for *Procedure* in the Assay. The relative retention times are about 0.7 for salicylic acid and 1.0 for aspirin. Calculate the percentage of salicylic acid ($C_7H_6O_3$) in the portion of Tablets taken by the formula:

$$2000(C/Q_A)\ (r_u/r_s),$$

in which C is the concentration, in mg per mL, of USP Salicylic Acid RS in the *Standard solution, Q_A* is the quantity, in mg, of aspirin ($C_9H_8O_4$) in the portion of Tablets taken, as determined in the *Assay*, and r_u and r_s are the peak responses of the salicylic acid peaks obtained from the *Test preparation* and the *Standard solution,* respectively: not more than 3.0% is found. In the case that are coated, not more than 3.0% 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.

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

Standard preparation-Dissolve an accurately weighed quantity of USP Aspirin RS in *Diluting solution* to obtain a solution having a known concentration of about 0.5 mg per mL.

Assay preparation-Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed quantity of the powder, equivalent to about 100 mg of aspirin, to a suitable container. Add 20.0 mL of *Diluting solution* and about 10 glass beads. Shake vigorously for about 10 minutes, and centrifuge (*stock solution*). Quantitatively dilute an accurately measured volume of the *Stock solution* with 9 volumes of *Diluting solution* (Assay preparation). Retain the remaining portion of *Stock solution* for the test for *Limit of salicylic acid*.

Chromatographic system (see *Chromatography* <621>)—The liquid chromatograph is equipped with a 280-nm detector and a 4.0-mm×30-cm column containing packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard*

preparation, and record the peak responses as directed under *Procedure*: the relative standard deviation is not more than 2.0%. In a suitable chromatogram, the tailing factor is not greater than 2.0.

Procedure-Separately inject equal volumes (about 10μL) 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 Tablets taken by the formula:

$$200C(r_U/r_S),$$

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 peak responses of the aspirin peaks obtained from the *Assay preparation* and the *Standard preparation*, respectively.