

QUININE SULFATE

Prepared at the 41st JECFA (1993), published in FNP 52 Add 2 (1993) superseding specifications prepared at the 39th JECFA (1992), published in FNP 54 Add 1 (1992). Not of toxicological concern at current uses levels up to 100 mg/l in soft drinks, 41st JECFA (1993)

DEFINITION

The sulfate of a natural substance, quinine, obtained from the bark of various species of cinchona including *Cinchona succirubra*, Pavon. (red cinchona); *Cinchona officinalis*, Linn; *Cinchona calizaya*, Wenddell; *Cinchona ledgeriana*, Moens.

Chemical names

(8S,9R)-6-methoxy-4-quinolenyl-5-vinyl-2-quinuclidinylmethanol sulfate dihydrate, quinine sulfate.
(8S,9R)-6'-methoxycinchonan-9-ol-sulfate dihydrate

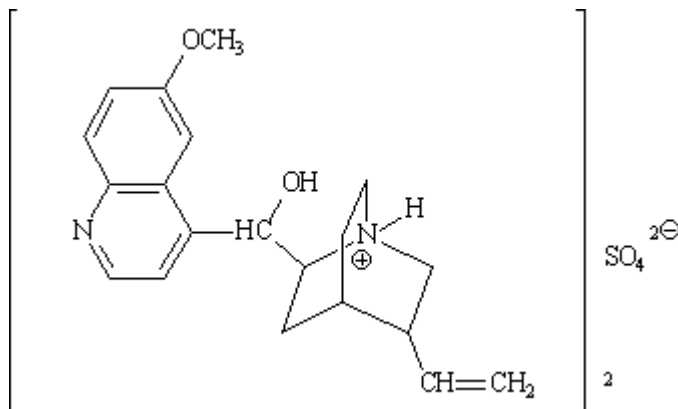
C.A.S. number

6119-70-6

Chemical formula

$(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4 \cdot 2H_2O$

Structural formula



Formula weight

782.96

Assay

Not less than 99.0% and not more than 101.0% on the dried basis

DESCRIPTION

Fine, white, needle-like crystals, usually lustreless, making a light and readily compressible mass; odourless; darkens on exposure to light

FUNCTIONAL USES

Flavouring agent

CHARACTERISTICS

IDENTIFICATION

Solubility (Vol. 4)

Slightly soluble in water at 25°, sparingly soluble at 100°; slightly soluble in ethanol at 25°, soluble at 80°; slightly soluble in chloroform; practically insoluble in ether

Specific rotation (Vol. 4)

$[\alpha]_{25, D}$: Between -240° and -248° (2% w/v solution in 0.1 N hydrochloric acid)

Fluorescence

Acidify a saturated solution of the sample with 10% sulfuric acid solution.

The resulting solution has intense blue fluorescence which disappears upon the addition of hydrochloric acid.

Colour test To 5 ml of a 1 in 1000 solution of the sample add 1 or 2 drops of bromine TS followed by 1 ml of ammonia TS. The liquid acquires an emerald green colour.

Test for sulfate (Vol. 4) Passes test

PURITY

Loss on drying (Vol. 4) Not less than 3% and not more than 5% (105°, 3h)

pH (Vol. 4) Between 5.7 and 6.6 (1 in 100 suspension in water)

Sulfated ash (Vol. 4) Not more than 0.05%
Test 2 g of the sample (Method I)

Chloroform-ethanol insoluble substances Not more than 0.1%
Warm 2 g of the sample with 15 ml of a mixture of 2 volumes of chloroform and 1 volume of absolute ethanol at 50° for 10 min. Filter through a tared, sintered-glass filter, and wash the filter with 10 ml portions of the chloroform-ethanol mixture. Dry at 105° for 1 h, cool and weigh.

Dihydroquinine sulfate Not more than 10%
See description under TESTS

Other cinchona alkaloids Agitate 1.8 g of the sample previously dried at 50° for 2 h, with 20 ml of water at 65° for 30 min. Cool the mixture to 15°, macerate it at this temperature for 2 h with occasional shaking, and then filter it through a filter paper (8 to 10 cm). Transfer 5 ml of the filtrate, at a temperature of 15° to a test tube and mix it gently, without shaking, with 6 ml of 10% ammonia solution (which must contain between 10 and 10.2% of NH₃, have a temperature of 15°, and be added at once). A clear liquid is produced.

Lead (Vol. 4) Not more than 2 mg/kg
Determine using an atomic absorption technique appropriate to the specified level. The selection of sample size and method of sample preparation may be based on the principles of the method described in Volume 4, "Instrumental Methods."

TESTS

PURITY TESTS

Dihydroquinine sulfate Place about 0.1 g of the sample accurately weighed, in a flask fitted with a ground glass stopper. Add 1 ml of 1 N hydrochloric acid. When the sample has dissolved add 10 ml of methanol and 10 ml of 0.1 N bromine. Close the flask and keep protected from light for 10 min, shaking gently from time to time. Rapidly add 20 ml of methanol, 3 ml of N potassium iodide solution and titrate with 0.1 N sodium thiosulfate using 1 ml of starch TS added towards the end of the titration as indicator. Carry out a blank determination. Calculate the content of dihydroquinine sulfate, in % by the

formula:

$$100 - \frac{1.867 \times (n_1 - n)}{p}$$

where

n = number of ml of 0.1 N sodium thiosulfate used in the test

n₁ = number of ml of 0.1 N sodium thiosulfate used in the blank

p = weight of sample in g

METHOD OF ASSAY

Dissolve about 200 mg of the sample, accurately weighed, in 20 ml of acetic anhydride, add 2 drops of 1% malachite green TS and titrate with 0.1N perchloric acid from a microburet to a yellow endpoint. Perform a blank determination. Each ml of 0.1 N perchloric acid is equivalent to 24.90 mg of $(C_{20}H_{24}N_2O_2)_2 \cdot H_2SO_4$.