QUININE HYDROCHLORIDE

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)

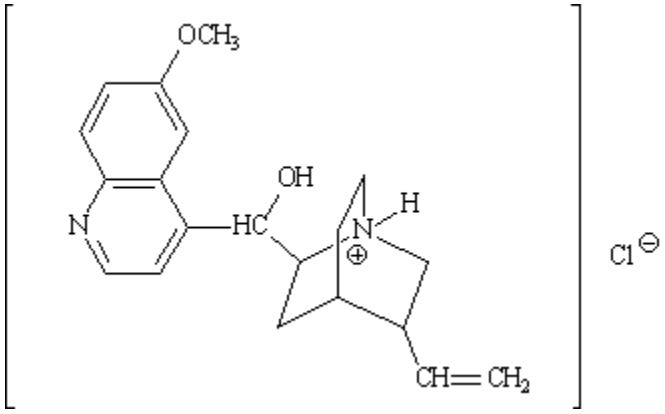
DEFINITION The hydrochloride of a natural substance, quinine, obtained from the bark of various species of Cinchona including *Cinchona succirubra*, Pavon. (red cinchona); *Cinchona officinalis*, Linn; *Cinchona calizaya*, Wenddell; *Cinchona ledgeriana*, Moens.

Chemical names (8S,9R)-6-methoxy-4-quinolenyl-5-vinyl-2-quinuclidinylmethanol hydrochloride dihydrate; (8S,9R)-6'-methoxycinchonan-9-ol-hydrochloride dihydrate

C.A.S. number 6119-47-7

Chemical formula $C_{20}H_{24}N_2O_2 \cdot HCl \cdot 2H_2O$

Structural formula



Formula weight 396.92

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

DESCRIPTION White, silky, glittering needles; odourless, effloresces when exposed to warm air

FUNCTIONAL USES Flavouring agent

CHARACTERISTICS

IDENTIFICATION

Solubility (Vol. 4) Soluble in water; very soluble in ethanol; freely soluble in chloroform; very slightly soluble in ether

Specific rotation (Vol. 4) [alpha] 25, D: Between -247° and -258° (2% w/v solution in 0.1 N 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 chloride (Vol. 4)	Passes test
PURITY	
Loss on drying (Vol. 4)	Not less than 6% and not more than 10% (105°, 3h)
pH (Vol. 4)	Between 6.0 and 6.8 (1 in 100 solution)
Sulfated ash (Vol. 4)	Not more than 0.1% Test 2 g of the sample (Method I)
Barium	To 10 ml of a hot solution of the sample (1 in 20) add 1 ml of dilute sulfuric acid TS. No turbidity is produced.
Sulfates (Vol. 4)	Not more than 0.05% Test 500 mg of sample as directed in the Limit Test using 0.5 ml of 0.01 N sulfuric acid in the control
Chloroform-ethanol insoluble substances	1 g of the sample dissolves completely in 7 ml of a mixture of 2 volumes of chloroform and 1 volume of absolute ethanol.
Dihydroquinine hydrochloride	Not more than 4% calculated on the basis of the dried substance See description under TESTS.
Foreign alkaloids	Dissolve 0.1 g of the sample in 2 ml of concentrated sulfuric acid and add 2 drops of concentrated nitric acid. No change in colour occurs.
Other cinchona alkaloids	Dissolve 1 g of the sample in 35 ml of boiling water and add to the boiling solution 6 ml of a 5% w/v solution of potassium chromate. Allow to cool for 3 h and filter through a sintered glass filter. Add to the clear filtrate 2 drops of sodium hydroxide TS. No visible change takes place in the solution. Heat the solution on a water bath for 1 h and then set aside for 24 h. The solution remains clear.
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 hydrochloride	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 hydrochloride, in % by the formula:

$$100 - \frac{1.804 \times (n_1 - n)}{p}$$

where
n = number of ml of 0.1 N sodium thiosulfate used in the test
n_1 = number of ml of 0.1 N sodium thiosulfate used in the blank
p = weight of sample in g

METHOD OF ASSAY

Dissolve about 150 mg of the sample, accurately weighed, in 20 ml of acetic anhydride, add 2 drops of malachite green TS and 5.5 ml of mercuric acetate TS and titrate with 0.1 N perchloric acid from a micro-buret to a yellow endpoint. Perform a blank determination and correct the sample titre as necessary. Each ml of 0.1 N perchloric acid is equivalent to 18.04 mg of $C_{20}H_{24}N_2O_2 \cdot HCl$.