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Chlortetracycline Bisulfate

(*This monograph has been updated to the current USP style. No revisions or changes to tests have been made.*)

DEFINITION

Chlortetracycline Bisulfate has a potency equivalent to NLT 760 µg/mg of chlortetracycline hydrochloride ($C_{22}H_{23}ClN_2O_8 \cdot HCl$), calculated on the dried and butyl alcohol-free basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Ultraviolet-Visible Spectroscopy*:** 197U

Medium: 0.1 N hydrochloric acid

Sample solution: 40 µg/mL

Wavelength: 368 nm

Acceptance criteria: Absorptivity, calculated on the dried and butyl alcohol-free basis, is NLT 83.0% and NMT 95.0% of that of USP Chlortetracycline Hydrochloride RS, the potency of the Reference Standard being taken into account.

ASSAY

• **Procedure**

Standard: USP Chlortetracycline Hydrochloride RS

Analysis: Proceed with Chlortetracycline Bisulfate as directed for chlortetracycline under *Antibiotics–Microbial Assays* ⟨81⟩.

Acceptance criteria: NLT 760 µg/mg of chlortetracycline hydrochloride on the dried and butyl alcohol-free basis

OTHER COMPONENTS

• **Sulfate Content**

Sample: 1 g of Chlortetracycline Bisulfate

Analysis: Transfer *Sample* to a 250-mL beaker, and dissolve in 100 mL of water. Neutralize the solution with 7.5 N ammonium hydroxide to litmus paper, and warm. Filter, and wash the filter with warm water. Neutralize the filtrate with 6 N hydrochloric acid to litmus, and add an additional 4 mL of 6 N hydrochloric acid. Heat the solution to boiling, and add, with constant stirring, sufficient boiling barium chloride TS to precipitate all of the sulfate. Add an additional 2 mL of barium chloride TS, and digest on a steam bath for 1 h. Pass the mixture through ashless filter paper, transferring the residue quantitatively to the filter, and wash the residue with hot water until no precipitate is obtained when 1 mL of silver nitrate TS is added to 5 mL of washing. Transfer the paper containing the residue to a tared crucible. Char the paper, without burning, and ignite the crucible and its contents to constant weight. Perform a blank determination concurrently with the *Sample* determination, and subtract the weight of the residue from that of the *Sample* determination to obtain the weight of the residue attributable to the sulfate content of the *Sample*.

Acceptance criteria: NLT 15.0%, calculated on the dried and butyl alcohol-free basis

IMPURITIES

• **Organic Impurities: Butyl Alcohol**

Solution A: 0.2 g/mL of ceric ammonium nitrate in 4 N nitric acid

Standard solution 1: 3 mg/mL of butyl alcohol in water

Standard solution 2: Transfer 10.0 mL of *Standard solution 1* and 1 drop of dimethicone to a 50-mL distilling flask equipped with a condenser and an extension that reaches into a collecting tube maintained in an ice-water bath. Distill slowly, and collect about 8 mL of distillate. Warm the distillate to ambient temperature, and transfer with the aid of water to a 10-mL volumetric flask. Dilute with water to volume and mix.

Sample solution: Transfer Chlortetracycline Bisulfate, equivalent to about 30 mg of butyl alcohol, to a 50-mL distilling flask equipped with a condenser and an extension that reaches into a collecting tube maintained in an ice bath. Add 25 mL of water and 1 drop of dimethicone to the distilling flask. Distill slowly, and collect about 8 mL of the distillate. Warm the distillate to ambient temperature, and transfer with the aid of water to a 10-mL volumetric flask. Dilute with water to volume and mix.

Spectrometric conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelength: Maximum absorbance, approximately 475 nm

Blank: Water

System suitability:

Samples: *Standard solution 1*, *Standard solution 2*, and *Blank*

To three separate test tubes add, respectively, 5.0 mL each of *Standard solution 1*, *Standard solution 2*, and *Blank*. To each add 2.0 mL of *Solution A* and mix.

Suitability requirements: The absorbance of the solution from *Standard solution 2* is NLT 98.0% of the absorbance of the solution from *Standard solution 1*.

Analysis

Samples: *Standard solution 1*, *Standard solution 2*, *Sample solution*, and *Blank*

To four separate test tubes add, respectively, 5.0 mL each of *Standard solution 1*, *Standard solution 2*, *Sample solution*, and *Blank*. To each add 2.0 mL of *Solution A* and mix.

Concomitantly determine the absorbances of the solutions from the *Standard solutions* and the *Sample solution* at the wavelength of maximum absorbance at about 475 nm, with a suitable spectrophotometer, using the *Blank* to set the instrument to zero.

Calculate the percentage of butyl alcohol in the portion of Chlortetracycline Bisulfate taken:

$$\text{Result} = (A_U/A_S) \times (W_S/W_U) \times 1000$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of *Standard solution 2*

W_S = weight of butyl alcohol taken to prepare *Standard solution 1* (g)

W_U = weight of Chlortetracycline Bisulfate taken to prepare *Sample solution* (mg)

Acceptance criteria: NMT 15.0%

SPECIFIC TESTS

- **Crystallinity ⟨695⟩:** Meets the requirements
- **Loss on Drying ⟨731⟩**

Analysis: Dry sample in a vacuum at a pressure not exceeding 5 mm of mercury at 60° for 3 h.

Acceptance criteria: NMT 2.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **Labeling:** Label it to indicate that it is intended for veterinary use only.
- **USP Reference Standards ⟨11⟩**

USP Chlortetracycline Hydrochloride RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
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REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BIO42020 Biologics Monographs 4 - Antibiotics

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