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Ivermectin Tablets

» Ivermectin Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of Ivermectin components H_2B_{1a} ($C_{48}H_{74}O_{14}$) plus H_2B_{1b} ($C_{47}H_{72}O_{14}$). They may contain a suitable antioxidant.

Packaging and storage—Preserve in well-closed containers, and store at a temperature below 30°.

USP Reference standards ⟨11⟩—

USP Ivermectin RS
USP 3-*tert*-Butyl-4-hydroxyanisole RS

Identification—The retention times of the H_2B_{1a} and H_2B_{1b} peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Dissolution ⟨711⟩—

Medium: 0.01 M phosphate buffer, pH 7, with 0.5% of sodium dodecyl sulfate (prepared by dissolving 50 g of sodium dodecyl sulfate in approximately 9 L of water, adding 100 mL of 1 M monobasic sodium phosphate monohydrate, adjusting with sodium hydroxide to a pH of 7, and diluting with water to 10 L); 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Determine the amount of $C_{48}H_{74}O_{14}$ (component H_2B_{1a}) plus $C_{47}H_{72}O_{14}$ (component H_2B_{1b}) dissolved by employing the following method.

Mobile phase—Prepare a degassed solution of acetonitrile, methanol, and water (53:35:12).

Standard stock solution—Prepare a 0.13 mg per mL solution of USP Ivermectin RS in *Medium*.

Standard solution—Using the accompanying table, dilute the *Standard stock solution* with *Medium* to volume, and mix.

Tablet Strength (mg per Tablet)	Required Dilution Ratio	Volume of *Standard stock solution* (mL)	Volumetric Flask Size (mL)
3.0	1 in 40	5.0	200
6.0	1 in 20	5.0	100

Test solution—Pass a portion of the solution under test through a suitable filter, and use the filtrate.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 245-nm detector and a 4.6-mm × 10-cm column that contains 5-µm packing L1. The flow rate is about 1.2 mL per minute. The column temperature is maintained at 30°.

Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.81 for H_2B_{1b} and 1.0 for H_2B_{1a}; the resolution, *R,* between the H_2B_{1a} and H_2B_{1b} peaks is not less than 1.5; the capacity factor, *k'*, for the H_2B_{1a} peak is not less than 4; the column efficiency determined from both the H_2B_{1a} and H_2B_{1b} peaks is not less than 1500 theoretical plates; the tailing factor for the H_2B_{1a} peak is not more than 2; and the relative standard deviation for replicate injections for the H_2B_{1a} peak is not more than 2.0%.

Procedure—Separately inject equal volumes (about 100 µL) of the *Test solution* and the *Standard solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the combined quantities, in percentage, of H_2B_{1a} plus H_2B_{1b} dissolved based on the peak responses obtained from the *Test solution* and the *Standard solution* by the formula:

$$[100(A_U)(W_S)(P)(D_U)]/[(A_S)(D_S)L]$$

in which A_U is the total peak area of H_2B_{1a} plus H_2B_{1b} obtained from the *Test solution; W_S* is the weight, in mg, of the USP Ivermectin RS taken to prepare the *Standard stock solution; P* is the purity of the USP Ivermectin RS (percent [w/w] H_2B_{1a} plus percent [w/w] H_2B_{1b}), expressed as a

decimal; D_U is the *Test solution* dilution factor; A_S is the total peak area of H_2B_{1a} plus H_2B_{1b} obtained from the *Standard solution;* D_S is the *Standard solution* dilution factor; and *L* is the label claim of ivermectin, in mg per Tablet.

Tolerances—Not less than 80% (*Q*) of the labeled amount of $C_{48}H_{74}O_{14}$ (H_2B_{1a}) plus $C_{47}H_{72}O_{14}$ (H_2B_{1b}) is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements for *Content uniformity*.

PROCEDURE FOR CONTENT UNIFORMITY—

Mobile phase—Prepare as directed in the *Assay*.

Standard solution A—Use the *Standard preparation* from the *Assay*.

Standard solution B—Dissolve an accurately weighed quantity of USP Ivermectin RS in methanol to obtain a solution containing 0.125 mg per mL.

Stock sensitivity solution (1%)—Use the *Stock sensitivity solution (1%)* from the *Assay*.

Sensitivity solution (0.2%)— Use the *Sensitivity solution (0.2%)* from the *Assay*.

Test solution—Transfer 1 Tablet into each of ten 25-mL volumetric flasks. Add 5.0 mL of water, and sonicate for 10 minutes. Add approximately 15 mL of methanol, sonicate for 5 minutes, and mix. Allow the solution to cool to room temperature. Dilute with methanol to volume, and mix. Pass a portion of each solution through a 1.0- to 1.2-µm chemically resistant filter prior to analysis.

Chromatographic system (see *Chromatography ⟨621⟩*)—Proceed as directed in the *Assay*.

Procedure—Separately inject equal volumes (about 10 µL) of *Standard solution A* (for the 6 mg per Tablet dose) or *Standard solution B* (for the 3 mg per Tablet dose), the *Sensitivity solution (0.2%)*, and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses of the ivermectin peaks. Calculate the quantity as a percentage of the label claim of ivermectin per Tablet taken by the formula:

$$[100(A_U)(W_S)(P)(D_U)]/[(A_S)(D_S)L]$$

in which A_U is the peak area of H_2B_{1a} plus the peak area of H_2B_{1b} obtained from the *Test solution;* W_S is the weight, in mg, of the USP Ivermectin RS taken to prepare *Standard solution A* or *Standard solution B; P* is the purity of USP Ivermectin RS (percent [w/w] H_2B_{1a} plus percent [w/w] H_2B_{1b}), expressed as a decimal; D_U is the *Test solution* dilution factor; A_S is the peak area of H_2B_{1a} plus the peak area of H_2B_{1b} obtained from *Standard solution A* or *Standard solution B;* D_S is the *Standard solution A* or *Standard solution B* dilution factor; and *L* is the label claim of ivermectin, in mg per Tablet.

Limit of 8a-oxo-H_2B_{1a}—

Mobile phase—Proceed as directed in the *Assay*.

BHA Working Standard solution—Dissolve an accurately weighed quantity of USP 3-*tert*-Butyl-4-hydroxyanisole RS in methanol, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of about 0.96 µg per mL.

Test solution—Use the *Assay preparation*.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The column temperature is maintained at 30°. The flow rate is about 1.2 mL per minute. Chromatograph the *BHA Working Standard solution* and the *Test solution,* and record the peak responses as directed for *Procedure:* the relative retention times at 280 nm are about 0.24 for BHA, 0.77 for 8a-oxo-H_2B_{1a}, and 1.0 for H_2B_{1a}.

Procedure—Separately inject equal volumes (about 10 µL) of the *BHA Working Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of 8a-oxo-H_2B_{1a} as a percentage of the label claim of ivermectin in the portion of Tablets taken by the formula:

$$[100(A_D)(W_S)(P)(D_U)(C_F)]/[(A_S)(D_S)(N)(L)(F)]$$

in which A_D is the peak area of 8a-oxo-H_2B_{1a} obtained from the *Test solution;* W_S is the weight of USP 3-*tert*-Butyl-4-hydroxyanisole RS, in mg, taken to prepare the *BHA Working Standard solution*; *P* is the purity of USP 3-*tert*-Butyl-4-hydroxyanisole RS, expressed as a decimal; D_U is the *Test solution* dilution factor; C_F is the correction factor (equal to 0.98) used to convert mg of 8a-oxo-H_2B_{1a} to mg of ivermectin; A_S is the peak area of BHA obtained from the *BHA Working Standard solution*; D_S is the *BHA Working Standard* solution dilution factor; *N* is the number of Tablets taken to prepare the *Test solution; L* is the label claim of ivermectin, in mg per Tablet; and *F* is the relative response factor (equal to 1.0): not more than 2.0% of 8a-oxo-H_2B_{1a} is found.

The correction factor, C_F, (equal to 0.98) is calculated by the following formula:

$$[0.90 \text{ (molecular weight of } H_2B_{1a}) + 0.10 \text{ (molecular weight of } H_2B_{1b})]/(\text{molecular weight of 8a-oxo-}H_2B_{1a}) = 873.10/889.10 = 0.98]$$

Assay—

Mobile phase—Prepare a mixture of acetonitrile, methanol, and water (53:35:12). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Dissolve an accurately weighed quantity of USP Ivermectin RS in methanol to obtain a solution containing 0.25 mg per mL.

Stock sensitivity solution (1%)—Quantitatively prepare a 1 in 100 dilution of the *Standard solution* in methanol.

Sensitivity solution (0.2%)—Quantitatively prepare a 1 in 5 dilution of the *Stock sensitivity solution (1%)* in methanol.

Assay preparation—Transfer the appropriate number of Tablets into a 250-mL volumetric flask according to the accompanying table:

Tablet Strength (mg per Tablet)	Number of Tablets
3.0	20
6.0	10

Add approximately 25 mL of water, and sonicate for 10 minutes. Add methanol to fill the flask three-quarters full, sonicate for 5 minutes or until the Tablets are completely disintegrated, and shake until mixed well. Allow the solution to cool to room temperature. Dilute with methanol to volume, add a magnetic stirrer, and mix until no lumps are present in the solution. Pass a portion of this solution through a 1.0- to 1.2-µm chemically resistant filter prior to injection.

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 245-nm detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.2 mL per minute. The column temperature is maintained at 30°. Chromatograph the *Sensitivity solution (0.2%)* and the *Standard preparation* at 245-nm detection, and record the peak responses as directed for *Procedure:* the signal-to-noise ratio for the ivermectin peak obtained from the *Sensitivity solution (0.2%)* is not less than 10; obtained from the *Standard preparation,* the relative retention times are about 0.82 and 1.0 for components H_2B_{1b} and H_2B_{1a}, respectively; the capacity factor, *k'*, for the component H_2B_{1b} is not less than 3; the column efficiency for component H_2B_{1a} is not less than 1500 theoretical plates; the tailing factor for component H_2B_{1a} is not more than 2; and the relative standard deviation for the area response for total ivermectin (H_2B_{1a} plus H_2B_{1b}) 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 peak areas for component H_2B_{1a} plus component H_2B_{1b}. Calculate the percentage of component H_2B_{1a} ($C_{48}H_{74}O_{14}$) plus component H_2B_{1b} ($C_{47}H_{72}O_{14}$) as a percentage of the label claim of ivermectin per Tablet taken by the formula:

$$[100(A_U)(W_S)(P)(D_U)]/[(A_S)(D_S)(N)(L)]$$

in which A_U is the total peak response of H_2B_{1a} plus H_2B_{1b} obtained from the *Assay preparation*; W_S is the weight of the USP Ivermectin RS, in mg, taken to prepare the *Standard preparation*; *P* is the purity of the USP Ivermectin RS (percent [w/w] H_2B_{1a} plus percent [w/w] H_2B_{1b}), expressed as a decimal; D_U is the sample dilution factor; A_S is the total peak area of H_2B_{1a} plus H_2B_{1b} obtained from the *Standard preparation;* D_S is the Standard dilution factor; *N* is the number of Tablets taken to prepare the *Assay preparation*; and *L* is the label claim of ivermectin, in mg per Tablet.

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

Topic/Question	Contact	Expert Committee
IVERMECTIN TABLETS	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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