

## <611> ALCOHOL DETERMINATION

### PROCEDURES

#### Method I—Distillation Method

Method I is to be used for the determination of alcohol, unless otherwise specified in the individual monograph. It is suitable for examining most fluidextracts and tinctures, provided the capacity of the distilling flask is sufficient (commonly two to four times the volume of the liquid to be heated) and the rate of distillation is such that clear distillates are produced.

Cloudy distillates may be clarified by agitation with talc, or with calcium carbonate, and filtered, after which the temperature of the filtrate is adjusted and the alcohol content determined from the specific gravity. During all manipulations, take precautions to minimize the loss of alcohol by evaporation.

Treat liquids that froth to a troublesome extent during distillation by rendering them strongly acidic with phosphoric, sulfuric, or tannic acid, or treat with a slight excess of calcium chloride solution or with a small amount of paraffin or silicone oil before starting the distillation.

Prevent bumping during distillation by adding porous chips of insoluble material such as silicon carbide, or beads.

**For liquids presumed to contain 30% of alcohol or less:** By means of a pipet, transfer to a suitable distilling apparatus not less than 25 mL of the liquid in which the alcohol is to be determined, and note the temperature at which the volume was measured. Add an equal volume of water, distill, and collect a volume of distillate about 2 mL less than the volume taken of the original test liquid, adjust to the temperature at which the original test liquid was measured, add sufficient water to measure exactly the original volume of the test liquid, and mix. The distillate is clear or not more than slightly cloudy, and does not contain more than traces of volatile substances other than alcohol and water. Determine the specific gravity of the liquid at 25°, as directed under *Specific Gravity* (841), using this result to ascertain the percentage, by volume, of C<sub>2</sub>H<sub>5</sub>OH contained in the liquid examined by reference to the *Alcoholometric Table* in the section *Reference Tables*.

**For liquids presumed to contain more than 30% of alcohol:** Proceed as directed in the foregoing paragraph, except to do the following: dilute the specimen with about twice its volume of water, collect a volume of distillate about 2 mL less than twice the volume of the original test liquid, bring to the temperature at which the original liquid was measured, add sufficient water to measure exactly twice the original volume of the test liquid, mix, and determine its specific gravity. The proportion of C<sub>2</sub>H<sub>5</sub>OH, by volume, in this distillate, as ascertained from its specific gravity, equals one-half that in the liquid examined.

#### Special Treatment

**Volatile acids and bases:** Render preparations containing volatile bases slightly acidic with diluted sulfuric acid before distilling. If volatile acids are present, render the preparation slightly alkaline with sodium hydroxide TS.

**Glycerin:** To liquids that contain glycerin add sufficient water so that the residue, after distillation, contains not less than 50% of water.

**Iodine:** Treat all solutions containing free iodine with powdered zinc before the distillation, or decolorize with just sufficient sodium thiosulfate solution (1 in 10), followed by a few drops of sodium hydroxide TS.

**Other volatile substances:** Spirits, elixirs, tinctures, and similar preparations that contain appreciable proportions of volatile materials other than alcohol and water, such as volatile oils, chloroform, ether, camphor, etc., require special treatment, as follows:

**For liquids presumed to contain 50% of alcohol or less:** Mix 25 mL of the specimen under examination, accurately measured, with about an equal volume of water in a separator. Saturate this mixture with sodium chloride, then add 25 mL of solvent hexane, and shake the mixture to extract the interfering volatile ingredients. Draw off the separated, lower layer into a second separator, and repeat the extraction twice with two further 25-mL portions of solvent hexane. Extract the combined solvent hexane solutions with three 10-mL portions of a saturated solution of sodium chloride. Combine the saline solutions, and distill in the usual manner, collecting a volume of distillate having a simple ratio to the volume of the original specimen.

**For liquids presumed to contain more than 50% of alcohol:** Adjust the specimen under examination to a concentration of approximately 25% of alcohol by diluting it with water, then proceed as directed in *For liquids presumed to contain 50% of alcohol or less*, beginning with "Saturate this mixture with sodium chloride."

In preparing *Collodion* or *Flexible Collodion* for distillation, use water in place of the saturated solution of sodium chloride directed above.

If volatile oils are present in small proportions only, and a cloudy distillate is obtained, the solvent hexane treatment not having been employed, the distillate may be clarified and rendered suitable for the specific gravity determination by shaking it with about one-fifth its volume of solvent hexane, or by filtering it through a thin layer of talc.

#### Method II—Gas Chromatographic Method

Use *Method IIa* when *Method II* is specified in the individual monograph. For a discussion of the principles upon which it is based, see *Gas Chromatography* under *Chromatography* (621).

##### • METHOD IIa

**Apparatus:** Under typical conditions, use a gas chromatograph equipped with a flame-ionization detector and a 4-mm × 1.8-m glass column packed with 100- to 120-mesh chromatographic column packing support S3, using nitrogen or heli-

um as the carrier. Prior to use, condition the column overnight at 235° with a slow flow of carrier gas. The column temperature is maintained at 120°, and the injection port and detector temperatures are maintained at 210°. Adjust the carrier flow and temperature so that acetonitrile, the internal standard, elutes in 5 to 10 minutes.

#### Solutions

**Test stock preparation:** Dilute the specimen under examination stepwise with water to obtain a solution containing approximately 2% (v/v) of alcohol.

**Test preparation:** Pipet 5 mL each of the *Test stock preparation* and the USP Alcohol Determination—Acetonitrile RS [NOTE—Alternatively, a 2% aqueous solution of acetonitrile of suitable quality may be used as the internal standard solution] into a 50-mL volumetric flask, dilute with water to volume, and mix.

**Standard preparation:** Pipet 5 mL each of the USP Alcohol Determination—Alcohol RS and the USP Alcohol Determination—Acetonitrile RS. [NOTE—Alternatively, a 2% aqueous solution of acetonitrile of suitable quality may be used as the internal standard solution] into a 50-mL volumetric flask, dilute with water to volume, and mix.

**Procedure:** Inject about 5 µL each of the *Test preparation* and the *Standard preparation*, in duplicate, into the gas chromatograph, record the chromatograms, and determine the peak response ratios. Calculate the percentage of alcohol (v/v) in the specimen under test according to the formula:

$$\text{Result} = CD(R_U/R_S)$$

$C$  = labeled concentration of USP Alcohol Determination—Alcohol RS

$D$  = dilution factor (the ratio of the volume of the *Test stock preparation* to the volume of the specimen taken)

$R_U$  = peak response ratio obtained from the *Test preparation*

$R_S$  = peak response ratio obtained from the *Standard preparation*

**System suitability test:** In a suitable chromatogram, the resolution factor,  $R$ , is not less than 2; the tailing factor of the alcohol peak is not greater than 2.0; and six replicate injections of the *Standard preparation* show a relative standard deviation of not more than 2.0% in the ratio of the peak of alcohol to the peak of the internal standard.

#### • METHOD IIB

**Apparatus:** The gas chromatograph is equipped with a split injection port with a split ratio of 5:1, a flame-ionization detector, and a 0.53-mm × 30-m capillary column coated with a 3.0-µm film of phase G43. Helium is used as the carrier gas at a linear velocity of 34.0 cm per second. The chromatograph is programmed to maintain the column temperature at 50° for 5 minutes, then to increase the temperature at a rate of 10° per minute to 200°, and maintain at this temperature for 4 minutes. The injection port temperature is maintained at 210° and the detector temperature at 280°.

#### Solutions

**Test stock preparation:** Dilute the specimen under examination stepwise with water to obtain a solution containing approximately 2% (v/v) of alcohol.

**Test preparation:** Pipet 5 mL each of the *Test stock preparation* and the USP Alcohol Determination—Acetonitrile RS [NOTE—Alternatively, a 2% aqueous solution of acetonitrile of suitable quality may be used as the internal standard solution] into a 25-mL volumetric flask, dilute with water to volume, and mix.

**Standard preparation:** Pipet 5 mL each of the USP Alcohol Determination—Alcohol RS and the USP Alcohol Determination—Acetonitrile RS. [NOTE—Alternatively, a 2% aqueous solution of acetonitrile of suitable quality may be used as the internal standard solution] into a 25-mL volumetric flask, dilute with water to volume, and mix.

**Procedure:** Inject about 0.2 to 0.5 µL each of the *Test preparation* and the *Standard preparation*, in duplicate, into the gas chromatograph, record the chromatograms, and determine the peak response ratios. Calculate the percentage of alcohol (v/v) in the specimen under test according to the formula:

$$\text{Result} = CD(R_U/R_S)$$

$C$  = labeled concentration of USP Alcohol Determination—Alcohol RS

$D$  = dilution factor (the ratio of the volume of the *Test stock preparation* to the volume of the specimen taken)

$R_U$  = peak response ratio obtained from the *Test preparation*

$R_S$  = peak response ratio obtained from the *Standard preparation*

**System suitability test:** In a suitable chromatogram, the resolution factor,  $R$ , between alcohol and the internal standard is not less than 4; the tailing factor of the alcohol peak is not greater than 2.0; and six replicate injections of the *Standard preparation* show a relative standard deviation of not more than 4.0% in the ratio of the peak of alcohol to the peak of the internal standard.

#### ADDITIONAL REQUIREMENTS

##### • USP REFERENCE STANDARDS (11)

USP Alcohol Determination—Acetonitrile RS

USP Alcohol Determination—Alcohol RS