Pharmaceutical Quality Management

ALCOHOLIC CONTENT DETERMINATION

By:

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INTRODUCTION:

- Ethanol content in pharmaceutics depends on formulation and varies in the wide range from fraction to tens of percent. The highest ethanol concentrations are characteristic for liquid formulations, including solutions, syrups, suspensions and emulsions. On the other hand, these preparations are most convenient for pediatric patients who are very often unable to swallow the solid preparations like capsules or tablets. It has reported that nearly 80% of pediatric medicines are produced as liquids and ethanol content in these products is in the range from 2.3 to 20%
- Alcohol is present as a major component in most of gelanicals

METHODS OF ALCOHOL DETERMINATION

I. DISTILLATION

II. GAS CHROMATOGRAPHY

II-a GAS CHROMATOGRAPHY

II-b GAS CHROMATOGRAPHY

Method I: Distillation method

- Method I must be used for the determination of alcohol, unless otherwise specified in individual monograph. This method is useful for examining most fluid extracts and tinctures, provided ; The capacity of the distilling flask is sufficient (commonly two to four times the volume of the liquid to be heated) Rate of distillation is such that clear distillates are produced
  - ***For liquids presumed to contain less than 30 % v/v alcohol***
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- Take 25 ml sample add equal volume of water and distillate.
- Collect distillate 2 ml less than original volume (23ml).
- Add water to make 25ml.
- Adjust temp and find specific gravity or refractive index.
- From Alcoholometric table find the %age of alcohol.

For liquids presumed to contain more than 30 % v/v alcohol

- Take 25ml sample add 50ml water and distillate.
- Collect distillate 2 ml less than 50ml (48ml).
- Add water to make 50ml.
- Adjust temp and find specific gravity or refractive index.
- From Alcoholometric table find the % age of alcohol.

  (the proportion of alcohol is ½ of liquid so multiply it with 2 to get exact % age of alcohol in sample)

Precautions of Distillation Method

Some precaution are taken

a. Distillate should be clear if cloudy add talc or $CaCO_3$ and filter, adjust temp.

b. Loss of alcohol should be minimized.

c. Size of the flask should be 3-4 time larger than volume of sample used.

d. Frothing should be avoided by adding H_3PO_4, H_2SO_4, tannic acid.

e. Bumping can be avoided by adding small pieces of broken glass, glass beads or porous chips.

Things to consider (special treatments)

- **Volatile acids & bases:** render the preparation containing volatile bases slightly acidic and vice versa.
- **Glycerin:** preparation should be diluted.
- **Iodine:** treat solutions with powdered zinc, decolorize with sod. thiosulphate add few drops of NaOH
- **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.*
  - ***For liquids presumed to contain 50% v/v alcohol or less.***
    - Mix 25 ml sample with equal volume of water in a separator.
    - Saturate with NaCl & add 25ml solvent hexane.
    - Shake well to remove any interfering volatile substance.
    - Draw lower layer and extract twice with hexane.
    - Extract this solution thrice with 10 ml portions of saturated saline.
    - Combine these portions and distil as usual
    - Take volume having simple ratio to original specimen.
  - ***For liquids presumed to contain more than 50% v/v alcohol.***
    - Adjust the conc. of alcohol to approximately 25% v/v by diluting with water.
    - Perform the same procedure as before.

Method 2: Gas Chromatography

Mainly two methods of gas chromatography in USP are used

II-a) Gas Chromatography

II-b) Gas Chromatography

Gas Chromatography

APPARATUS:

Under typical conditions, use a gas chromatograph quipped 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 helium as the carrier.

Prior to use, condition the column overnight at 235°C with a slow flow of carrier gas. The column temperature is maintained at 120°C, and the injection port and detector temperatures are maintained at 210°C. 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:

$$\%\text{age of alcohol} = CD(RU/RS)$$

- In which C is the labeled concentration of USP Alcohol Determination—Alcohol RS; D is the dilution factor (the ratio of the volume of the Test Stock Preparation to the volume of the specimen taken); and RU and RS are the peak response ratios obtained from the Test Preparation and the Standard Preparation, respectively.

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 (%RSD) of not more than 2.0% in the ratio of the peak of alcohol to the peak of the internal standard.