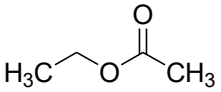
Ethyl Acetate



$C_4H_8O_2$ Mol. Wt. 88.1

Ethyl Acetate is Acetic acid, ethyl ester.

Ethyl Acetate contains not less than 98.0 per cent and not more than 102.0 per cent of $C_4H_8O_2$.

Category. Excipient.

Description. A transparent, colourless liquid.

Identification

Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *ethyl acetate IPRS* or with the reference spectrum of ethyl acetate.

Test

Specific gravity (2.4.29). 0.894 to 0.898.

Acidity. To 2.0 ml, add 10 ml of neutralized *ethanol*, add 2 drops of *phenolphthalein* solution. Neutralize with *0.1M sodium hydroxide*. Not more than 0.1 ml of *0.1 M sodium hydroxide* is required to change the colour of the solution.

Readily carbonizable substances. To 2.0 ml, add 10.0 ml of *sulphuric acid* to form separate layers. No dark zone is developed within 15 minutes.

Limit of nonvolatile residue. Not more than 0.02 per cent, determined by evaporating 100 g of Ethyl Acetate to dryness in a tared porcelain dish on a steam-bath and dry at 105° for 1 hour.

Related substances. Determine by gas chromatography (2.4.13).

Test solution. Dissolve 1.6 g of Ethyl Acetate in10.0 ml of *N,N-dimethylacetamide*.

Reference solution (a). A solution containing 0.016 per cent w/v, each of, *acetaldehyde* and *methanol,* 16.0 per cent w/v of *ethyl acetate IPRS* and 0.16 per cent w/v of *methyl ethyl ketone IPRS* in *N,N-dimethylacetamide*.

Reference solution (b). A solution containing 0.016 per cent w/v, each of, *acetaldehyde*, *ethyl acetate IPRS* and *1-ethoxy-2-methylpropane IPRS* in *N,N-dimethylacetamide.*

Reference solution (c). A solution containing 0.016 per cent w/v, each of, *methanol, methyl acetate*, and *methyl isobutyrate* in *N,N-dimethylacetamide* (For identification of Methyl compounds).

Reference solution (d). Dilute 5.0 ml of reference solution (b) to 10.0 ml with *N,N-dimethylacetamide.*

Chromatographic system

- a fused-silica capillary column 60 m x 0.32 mm coated with 6 per cent cyanopropylphenyl- 94 per cent dimethylpolysiloxane (film thickness 1.8 µm) (Such as DB 624),
- temperature:
  column. 40° for 15 minutes, 40° to 200° @ 12° per minute and hold at 200° for 2 minutes,
- inlet port at 210° and detector at 250°,
- flame ionisation detector,
- flow rate: 3 ml per minute using nitrogen as carrier gas,
- split ratio of 30:1,
- injection volume: 1 µl.

Name	Relative retention time
Acetaldehyde	0.29
Methanol	0.31
Methyl ethyl ketone	0.97
Ethyl acetate	1.0

Inject reference solution (a), (b) and (d). The test is not valid unless the resolution between the peaks due to acetaldehyde and methanol is not less than 2.0 and between the peaks due to methyl ethyl ketone and ethyl acetate is not less than 2.0 in the chromatogram obtained with reference solution (a), the relative standard deviation for replicate injections is not more than 5.0 per cent and the tailing factor is not more than 1.5 for acetaldehydes ethylacetate and 1-ethoxy-2-methylpropane peaks in the chromatogram obtained with reference solution (b) and signal-to-noise ratio for acetaldehyde, ethyl acetate, and 1-ethoxy-2-methylpropane peaks is not less than 20 in the chromatogram obtained with reference solution (d).

Inject reference solution (c) to identify the peaks due to methanol, methyl acetate and methyl isobutyrate.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to acetaldehyde and 1-ethoxy-2-methylpropane, each of, is not more than the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.1 per cent), the sum of the areas of the peaks corresponding to methyl compound (methanol, methyl acetate and methyl isobutyrate) multiplied by correction factor 0.1 is not more than the area of the ethyl acetate peak in the chromatogram obtained with reference solution (b) (0.1 per cent) and the sum of the areas of all the secondary peaks other than acetaldehyde, 1-ethoxy-2-methylpropane and methyl compounds is not more than 3 times the area of the ethyl acetate peak in the chromatogram obtained with reference solution (b) (0.3 per cent).

Bacterial endotoxins (2.2.3). If labeled for use in preparing parenteral dosage forms, it also meets the following requirements. The level of bacterial endotoxins is such that the requirement in the relevant dosage form monographs in which Ethyl Acetate is used can be met. Where the label states that Ethyl Acetate must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins is such that the requirement in the relevant dosage form monograph in which Ethyl Acetate is used can be met.

Assay. Determine by gas chromatography (2.4.13).

Test solution. Dissolve 50 mg of Ethyl Acetate in 25.0 ml of *N,N-dimethylacetamide*.

Reference solution (a). A solution containing 0.2 per cent w/v of *ethyl acetate IPRS* and 0.002 per cent w/v of *methyl ethyl ketone IPRS* in *N,N-dimethylacetamide.*

Reference solution (b). A 0.2 per cent w/v solution of *ethyl acetate IPRS* in *N,N-dimethylacetamide.*

Use chromatographic system as described under Related substances.

The relative retention time with reference to ethyl acetate for methyl ethyl ketone is about 0.97.

Inject reference solution (a), (b). The test is not valid unless the resolution between the peaks due to methyl ethyl ketone and ethyl acetate is not less than 2.0 in the chromatogram obtained with reference solution (a), the tailing factor is not more than 1.5 and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (b).

Inject reference solution (b) and the test solution.

Calculate the content of $C_4H_8O_2$.

Storage. Store protected from moisture, at a temperature not exceeding 30°.

Labelling. When it is intended for use in preparing injectable dosage forms, the label states that it must be subjected to further processing during the preparation of injectable dosage forms to ensure acceptable levels of bacterial endotoxins.

Solubility. Soluble in *water,* miscible with *ethanol, ether,* fixed oils and with volatile oils.

4.2. General reagent

Methyl isobutyrate: $C_5H_{10}O_2$ = 102.13

General laboratory reagent grade of commerce.