Etophylline

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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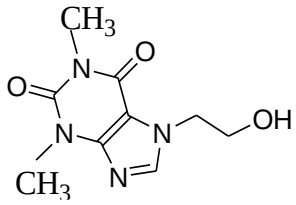
Etophylline



$C_9H_{12}N_4O_3$ Mol. Wt. 224.2

Etophylline is 7-(2-hydroxyethyl)-1,3-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione.

Etophylline contains not less than 98.5 per cent and not more than 101.0 per cent of $C_9H_{12}N_4O_3$, calculated on the dried basis.

Category. Bronchodilator

Description. A white or almost white, crystalline powder.

Identification

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

B. Melting point (2.4.21). 161° to 166°.

C. It gives the reaction of xanthines (2.3.1).

Tests

Appearance of solution. A 5.0 per cent w/v solution in *carbon dioxide-free water* (solution A) is clear (2.4.1) and colourless (2.4.1).

Acidity or alkalinity. To 10 ml of solution A, add 0.25 ml of *bromothymol blue solution*. The solution is yellow or green. Not more than 0.4 ml of *0.01 M sodium hydroxide* is required to change the colour of the indicator to blue.

Related substances. Determine by thin-layer chromatography (2.4.17), coating the plate with *silica gel* HF_{254}.

NOTE — Prepare the solutions immediately before use.

Mobile phase. A mixture of 90 volumes of *chloroform*, 10 volumes of *ethanol* and 1 volume of *ammonia*.

Test solution. Dissolve 0.3 g of the substance under examination in a mixture of 40 volumes of *water* and 60 volumes of *methanol* and dilute to 10.0 ml with the same solvent.

Reference solution (a). A 3.0 per cent w/v solution of *etophylline IPRS* in a mixture of 40 volumes of *water* and 60 volumes of *methanol*.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with *methanol*.

Reference solution (c). Dilute 0.2 ml of reference solution (a) to 100.0 ml with *methanol*.

Reference solution (d). Dissolve 10 mg of *theophylline IPRS* in *methanol*, add 0.3 ml of reference solution (a) and dilute to 10.0 ml with *methanol*.

Apply to the plate 10 µl of each solution. Allow the mobile phase to rise 15 cm and examine under ultraviolet light at 254 nm. Any secondary spot in the chromatogram obtained with the test solution is not more intense than the spot in the chromatogram obtained with reference solution (b) (1.0 per cent) and one such spot is more intense than the principal spot in the chromatogram obtained with reference solution (c) (0.2 per cent). The test is not valid unless the chromatogram obtained with reference solution (d) shows two clearly separated spots.

Chlorides (2.3.12). 0.625 g complies with the limit test for chlorides (400 ppm).

Heavy metals (2.3.13). 1.0 g complies with limit test for heavy metals, Method B (20 ppm).

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Loss on drying (2.4.19). Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105°.

Assay.

Note-In order to avoid overheating in the reaction medium, mix thoroughly throughout and stop the titration immediately after the end-point has been reached.

Dissolve 0.2 g of the substance under examination in 3 ml of *anhydrous formic acid* and add 50 ml of *acetic anhydride*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (2.4.25).

1 ml of *0.1 M perchloric acid* is equivalent to 0.02242 g of $C_9H_{12}N_4O_3$.

Storage. Store protected from light.

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Solubility: Soluble in *water* and slightly soluble in *ethanol*.