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Theophylline Prolonged-release Tablets

General Notices

Prolonged-release Theophylline Tablets

Theophylline Prolonged-release Tablets from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Non-selective phosphodiesterase inhibitor (xanthine); treatment of reversible airways obstruction.

DEFINITION

Theophylline Prolonged-release Tablets contain Theophylline or Theophylline Hydrate. The are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Theophylline. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of theophylline, $C_7H_8N_4O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. In the Assay, the chromatogram obtained with solution (1) shows a peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).
B. Extract a quantity of the powdered tablets containing the equivalent of 0.2 g of theophylline with 10 mL of a mixture of 60 volumes of *chloroform* and 40 volumes of *methanol*, filter and evaporate the filtrate to dryness. The residue yields the reaction characteristic of *xanthines*, Appendix VI.

TESTS

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using a *TLC silica gel F_{254} plate* and a mixture of 10 volumes of *concentrated ammonia*, 30 volumes of *acetone*, 30 volumes of *chloroform* and 40 volumes of *butan-1-ol* as the mobile phase. Apply separately to the plate 10 µL of each of the following solutions. For solution (1) mix with the aid of ultrasound a quantity of the powdered tablets containing the equivalent of 0.2 g of theophylline with 10 mL of a mixture of 60 volumes of *chloroform* and 40 volumes of *methanol* and centrifuge. For solution (2) dilute 1 volume of solution (1) to 200 volumes with a mixture of 60 volumes of *chloroform* and 40 volumes of *methanol*. After removal of the plate, allow it to

dry in air and view under *ultraviolet light (254 nm)*. Any *secondary spot* in the chromatogram obtained with solution (1) is not more intense than the principal spot in the chromatogram obtained with solution (2) (0.5%).

ASSAY

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. For solution (1) add 1 mL of *methanol* to a quantity of the powdered tablets containing the equivalent of 0.1 g of theophylline, mix and add 50 mL of *water*. Dissolve with the aid of ultrasound, swirling occasionally, dilute to 100 mL with *water* and mix thoroughly. Dilute 5 mL to 50 mL with *water*. Solution (2) contains 0.01% w/v of *theophylline BPCRS* in water.

The chromatographic procedure may be carried out using (a) a stainless steel column (30 cm × 3.9 mm) packed with *octadecylsilyl silica gel for chromatography* (10 µm) (µBondapak C18 is suitable), (b) as the mobile phase with a flow rate of 1.8 mL per minute a mixture of 250 volumes of *methanol* and 750 volumes of *water* and (c) a detection wavelength of 270 nm.

Calculate the content of $C_7H_8N_4O_2$ in the tablets using the declared content of $C_7H_8N_4O_2$ in *theophylline BPCRS*.

LABELLING

When the active ingredient is Theophylline Hydrate the quantity is stated in terms of the equivalent amount of theophylline.