Dextropropoxyphene Hydrochloride and Paracetamol Tablets

Co-proxamol Tablets

Dextropropoxyphene Hydrochloride and Paracetamol Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amounts of dextropropoxyphene hydrochloride, $C_{22}H_{29}NO_2$,HCl and paracetamol, $C_8H_9NO_2$.

Usual strength. Paracetamol, 300 mg and Dextropropoxyphene Hydrochloride, 25 mg.

Identification

A. Disperse a quantity of the powdered tablets containing about 0.1 g of Dextropropoxyphene Hydrochloride in 20 ml of *0.1M hydrochloric acid*, with the aid of ultrasound for 5 minutes and filter. To the filtrate, add 5 ml of *2 M sodium hydroxide*, extract twice with 25 ml quantities of *dichloromethane*, wash the combined extracts with 10 ml of *water*, shake with *anhydrous sodium sulphate,* filter and evaporate the filtrate to dryness. Dissolve the residue in 2 ml of *dichloromethane* and add 50 µl of the solution, drop wise, onto the surface of a disc prepared from about 0.3 g of *potassium bromide*, evaporate the solvent, dry the disc at 50º for 2 minutes. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *dextropropoxyphene hydrochloride IPRS* treated in the same manner or with the reference spectrum of dextropropoxyphene.

B. Disperse a quantity of the powdered tablets containing 0.325 g of Paracetamol in 10 ml of *acetone*, with the aid of ultrasound for 5 minutes, filter and evaporate the filtrate to dryness. On the residue, determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *paracetamol IPRS* or with the reference spectrum of paracetamol.

Tests

For Paracetamol-

Dissolution (2.5.2).

Apparatus. No 2 (Paddle),
Medium. 900 ml of *phosphate buffer pH 5.8*,
Speed and time. 50 rpm and 45 minutes.

Withdraw a suitable volume of the medium, filter and dilute a suitable volume of the filtrate with *0.1M sodium hydroxide*, if necessary, to obtain a solution containing 0.00075 per cent w/v of paracetamol. Measure the absorbance of the resulting solution at the maximum at about 257 nm (2.4.7). Calculate the content of $C_8H_9NO_2$ taking 715 as the specific absorbance at 257 nm.

Q. Not less than 70 per cent of the stated amount of $C_8H_9NO_2$.

4-Aminophenol. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of the powdered tablets containing 0.5 g of Paracetamol in the mobile phase, with the aid of ultrasound and dilute to 50.0 ml with the mobile phase.

Reference solution. A 0.001 per cent w/v solution of *4-aminophenol IPRS* in the mobile phase.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (10 µm) (Nucleosil C18),
- mobile phase: *0.01M sodium butane sulphonate* in a mixture of 85 volumes of *water*, 15 volumes of *methanol* and 0.4 volume of *formic acid*,
- flow rate: 2 ml per minute,
- spectrophotometer set at 272 nm,
- injection volume: 20 µl.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution the area of any peak corresponding to 4-aminophenol is not more than the area of the principal peak in the chromatogram obtained with the reference solution (0.1 per cent).

Related substances.

For Dextropropoxyphene Hydrochloride –

Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of the powdered tablets containing 25 mg of Dextropropoxyphene Hydrochloride in 5 ml of *acetonitrile* by shaking for 2 minutes, add 5 ml of *water* and further shake for 5 minutes, dilute to 25.0 ml with *water*, filter.

Reference solution. A solution containing 0.0005 per cent w/v, each of, *4-dimethylamino-3-methyl-1, 2-diphenylbutan-2-olhydrochloride IPRS* and *(1S, 2R)-1-benzyl-3-dimethylamino-2-methyl-1-phenylpropyl acetate IPRS* in a mixture of 1 volume of *acetonitrile* and 4 volumes of *water*.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Nucleosil C18),
- mobile phase: a mixture of 40 volumes of *acetonitrile* and 60 volumes of *0.2M sodium perchlorate*, previously adjusted to pH 2.0 with *7M hydrochloric acid,*
- flow rate: 2 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to 4-dimethylamino-3-methyl-1, 2-diphenylbutan-2-olhydrochloride and (1S, 2R)-1-benzyl-3-dimethylamino-2-methyl-1-phenylpropyl acetate is not less than 1.5.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peaks corresponding to 4-dimethylamino-3-methyl-1,2-diphenylbutan-2-olhydrochloride and (1S, 2R)-1-benzyl-3-dimethylamino-2-methyl-1-phenylpropyl acetate, each of, is not more than the area of the corresponding peaks in the chromatogram obtained with the reference solution (0.5 per cent).

For Paracetamol –

Determine by thin-layer chromatography (2.4.17), coating the plate with *silica gel GF254*.

Mobile phase. A mixture of 10 volumes of *toluene*, 25 volumes of *acetone* and 65 volumes of *chloroform.*

Test solution (a). Disperse a quantity of powdered tablets containing 1.0 g of Paracetamol in 5 ml of *peroxide free ether*, shake for 30 minutes, centrifuge at 1000 revolution per minute for 15 minutes or until a clear supernatant liquid is obtained and use the supernatant liquid.

Test solution (b). Dilute 1.0 ml of test solution (a) to 10.0 ml with *ethanol* (*95 per cent*).

Reference solution (a). A 0.005 per cent w/v solution of *4-chloroacetanilide IPRS* in *ethanol* (*95 per cent*).

Reference solution (b). A solution containing 0.25 per cent w/v of *4-chloroacetanilide IPRS* and 0.1 per cent w/v of *paracetamol IPRS* in 100.0 ml *ethanol (95 per cent)*.

Apply to the plate 200 µl of test solution (a) and 40 µl, each of test solution (b), reference solution (a) and reference solution (b). Allow the mobile phase to rise 14 cm. Dry the plate in hot air and examine under ultraviolet light at 254 nm. In the chromatogram obtained with test solution (a), any spot corresponding to 4-chloroacetanilide is not more intense than the principal spot in the chromatogram obtained with the reference solution (a) (0.005 per cent). In the chromatogram obtained with test solution (b), any secondary spot with an Rf value lower than that of 4-chloroacetanilide is not more intense than the principal spot in the chromatogram obtained with the reference solution (b) (0.25 per cent). The test is not valid unless two clearly separated spots are seen in the chromatogram obtained with reference solution (b), the spot corresponding to 4-chloroacetanilide having he higher Rf value.

Other tests. Comply with the tests stated under Tablets

Assay.

For Dextropropoxyphene Hydrochloride –

Determine by liquid chromatography (2.4.14)
Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 32.5 mg of Dextroprpoxyphene Hydrochloride in 100 ml of *0.02 M hydrochloric acid*, with aid of ultrasound for 15 minutes, dilute to 500.0 ml with a mixture of equal volume of *acetonitrile* and *0.02 M hydrochloric acid* and filter.

Reference solution (a). A 0.0065 per cent w/v solution of *dextropropoxyphene hydrochloride IPRS* in a mixture of 40 volumes of *acetonitrile* and 60 volumes of *0.02 M hydrochloric acid*.

Reference solution (b). A solution containing 0.0005 per cent w/v solution, each of, *4-dimethylamino-3-methyl-1, 2-diphenylbutan-2-olhydrochloride IPRS* and *(1S, 2R)-1-benzyl-3-dimethylamino-2-methyl-1-phenylpropyl acetate IPRS* in a mixture of 1 volume of *acetonitrile* and 4 volume of *water*.

Chromatographic system

– a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Nucleosil C18),
– mobile phase: a mixture of 40 volumes of *acetonitrile* and 60 volumes of *0.2 M sodium perchlorate*, previously adjusted to pH 2.0 with *7M hydrochloric acid*.
– flow rate: 2 ml per minute,
– spectrophotometer set at 215 nm,
– injection volume: 20 µl.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to 4-dimethylamino-3-methyl-1, 2-diphenylbutan-2-olhydrochloride and *(*1S, 2R)-1-benzyl-3-dimethylamino-2-methyl-1-phenylpropyl acetate is not more than 1.5

Inject reference solution (a) and the test solution.

Calculate the content of $C_{22}H_{29}NO_2$.HCl in the tablets.

For Paracetamol –

Disperse a quantity of powdered tablets containing 325 mg of Paracetamol in 5 ml of *water*, add 100 ml of *methanol* and shake. Add 300 ml of *water,* shake for 5 minutes and dilute to 500.0 ml with *water*, mix and filter. Dilute 5.0 ml of the filtrate to 250.0 ml with *0.1 M sodium hydroxide*. Measure the absorbance of the resulting solution at the maximum at about 257 nm (2.4.7). Calculate the content of $C_8H_9NO_2$ in the tablets taking 715 as the specific absorbance at 257 nm.

Storage. Store protected from light.