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Determination of dihydroxypropyltheophylline in plasma

There are numerous methods in the literature for the detection of dihydroxypropyltheophylline (diprophylline) in various solutions, but none are sensitive enough for its determination in plasma after therapeutic doses (Bukowska & Gierlowska, 1960, Ott & Wittman-Zinke, 1958; Raber, 1964).

The procedure of Schack & Waxler (1949) for theophylline has now been modified for the determination of diprophylline in plasma.

The procedure involves an extraction of the drug from plasma into chloroform–isopropanol (10:1) from which the drug is re-extracted with 20% v/v sulphuric acid. The absorbance of this solution is then read in a spectrophotometer. The absorbance of a standard solution of the drug in 20% v/v sulphuric acid is also measured. The peak absorbance is at 268 nm. The absorbance peak for theophylline in 0·1 N sodium hydroxide is at 277 nm.

Method. Plasma (2·0 ml) is extracted with chloroform (spectrograde)—isopropanol (nanograde) (10:1) (50 ml) by shaking vigorously for 10 min in a 120 ml separatory funnel. The solvent layer is then filtered through anhydrous sodium sulphate, the filter washed with fresh solvent (1 ml) and the filtrates combined. The plasma (aqueous) layer is then extracted a second time with another portion of chloroform-isopropanol (50 ml) for 10 min and the organic layer filtered to remove water as above and added to the previous 50 ml portion. The combined solvent layers (102 ml) are evaporated on a water bath to a final volume of 10 ml. This is placed in a 30 ml vial and extracted with 20% v/v sulphuric acid (reagent grade; 4·0 ml) by shaking vigorously for 10 min. The vial is then centrifuged to break the slight emulsion that forms. The sulphuric acid layer is pipetted into a cuvette and the absorbance read at 268 nm against a reagent blank consisting of plasma samples without diprophylline treated in the same way as the samples.

The percent recovery of diprophylline is 85–90% in the range of 10·0 to 50·0 μg/ml of plasma. The method is equally effective for human and rat plasma, is simple and fairly rapid and inexpensive.

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