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Note

Analysis of promazine in pharmaceutical preparations by high-performance liquid chromatography

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Promazine is a phenothiazine drug closely related to the major tranquiliser chlorpromazine (Fig. 1). It has been used for the treatment of psychoses but has been found to be useful in the treatment nausea and vomiting associated with pregnancy[1]. Promazine is available in tablet form, as a suspension and as an intramuscular or intravenous injection. As with other phenothiazines, promazine undergoes aerial oxidation in the presence of light to produce a sulphoxide[2]. This degradation is particularly apparent in liquid preparations stored in partially filled containers. The present method employed for the determination of promazine sulphoxide in the presence of the intact drug is that of difference spectrophotometry[3]. This method involves the measurement of the absorbance of a solution of the sulphoxide in 0.2 *M* hydrochloric acid relative to an equimolar solution reduced with zinc dust to give promazine.

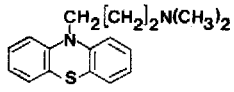

Fig. 1. The structure of promazine.

This paper reports a rapid high-performance liquid chromatographic (HPLC) method which allows the analysis of both promazine and its sulphoxide degradation product in pharmaceutical preparations. The analysis of chlorpromazine by reversed-phase HPLC has encountered problems due to severe peak tailing. This problem has been circumvented either by the use of basic eluents[4,5] or by the addition of an ion-pair agent, such as sodium lauryl sulphate[6], to the eluent. Both of these techniques were investigated for the analysis of promazine using a Spherisorb 5 μm ODS column. However, neither produced any improvement in peak shape. Far better results were obtained by the use of adsorption chromatography employing a silica column.

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EXPERIMENTAL

Apparatus

The chromatographic system consisted of a Spectra Physics 8700 XR extended range LC pump which was used to deliver solvent at 1.5 ml/min. The eluent was monitored at 240 nm with a Pye Unicam PU4020 variable-wavelength ultraviolet detector. The column (25 cm × 4.5 mm I.D.) was packed with Spherisorb 5 μm (Jones Chromatography) and fitted with a Negretti and Zambra injection system incorporating a 20-μl loop. Separation was achieved with an eluent of 25% aqueous ammonium acetate (5%, w/v) to pH 9.5 with ammonia solution and 75% methanol. All solvents used were of HPLC grade (Rathburn Chemicals).

Materials

Promazine hydrochloride was obtained from Wyeth Pharmaceuticals. Promazine sulphoxide was produced by the oxidation of promazine by the addition of peroxyacetic acid. Peroxyacetic acid was generated by the addition of dilute hydrogen peroxide (100 volumes) 1 ml to 100 ml with glacial acetic acid. The solution was heated at 70°C for 1 h prior to use. The oxidising agent (1 ml) was added to 1 ml of aqueous solution of promazine hydrochloride (1 mg/ml). Oxidation was allowed to proceed for 1 h at 70°C prior to dilution of the mixture with distilled water and analysis by HPLC. Pharmaceutical preparations of promazine were obtained from Wyeth Pharmaceuticals.

Procedures

Promazine tablets (25 mg) were crushed and dissolved in sufficient distilled water to give a final concentration of approximately 200 μg/ml. Aliquots (20 μl) of this solution were injected directly on to the column. Suspensions (10 mg/ml) and injections (50 mg/100 ml) were similarly diluted with distilled water to a final concentration of about 200 μg/ml prior to analysis.

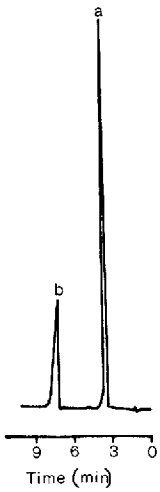

Fig. 2. Chromatogram of a partially degraded solution of promazine showing the separation of promazine (a) and promazine sulphoxide (b).

A straight-line calibration graph was constructed for promazine based on peak area measurements for concentrations of 50, 100, 200 and 400 μg/ml in distilled water. Each point was taken as the average of two determinations.

RESULTS AND DISCUSSION

A chromatogram of a partially oxidised solution of promazine is represented in Fig. 2. A good separation was achieved between the parent drug and its sulphoxide degradation product. A straight-line calibration graph for promazine was determined as $y = 0.052\,x - 0.0217$ with a correlation coefficient of 1.0. The limit of detection (signal-to-noise ratio > 2) was approximately 1 ng on column.

The presence of diluents and excipients in the pharmaceutical preparations examined did not interfere with the analysis of promazine and promazine sulphoxide. This method, therefore, allows the direct analysis of pharmaceuticals containing promazine without extraction of the drug and without the necessity of a reduction stage. The assay provides a rapid method for the quality control of preparations of promazine.

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