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HIGH PRESSURE LIQUID CHROMATOGRAPHIC ASSAY FOR HALOPERIDOL

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ABSTRACT

A high pressure liquid chromatographic assay for haloperidol in aqueous solutions is presented. This assay permits the separation and quantitation of drug concentrations below 100 ng/ml.

INTRODUCTION

The current USP XIX assay for haloperidol involves titration of haloperidol with 0.05N perchloric acid.[1] Problems associated with the establishment of titration endpoints can make the measurement of drug concentration difficult. Further, the USP assay gives little information on the presence and amount of contaminants and degradation products. A high pressure liquid chromatographic assay for haloperidol

with ultraviolet detection has been developed to enable the separation and rapid quantitation of the drug in aqueous solutions.

EXPERIMENTAL

Material

Haloperidol was obtained from McNeil Pharmaceutical Company (Fort Washington, PA). Tetrahydrofuran (UV Grade) was purchased from Waters Associates (Milford, MA). Phosphoric acid was obtained from Fisher Scientific (Boston, MA).

High Pressure Liquid Chromatograph

A constant flow solvent delivery system (Waters Associates M-6000A) was connected to a fixed loop injector fitted with a fifty microliter loop (Rainin 7120, Berkeley, CA). A bonded phase reverse phase column (Waters microBondapak CN) was used for all separations. Detection of column effluent was performed using a flow through ultraviolet detector at a fixed wavelength of 254 nm (Waters Associates 440). The output of the detector was recorded on a Linear Systems 8373-10 strip chart recorder.

Methods

A mobile phase consisting of 44% tetrahydrofuran and 0.75% phosphoric acid in water was supplied by the solvent delivery system at a constant flow rate

of 1.0 ml/min. Haloperidol was prepared in mobile phase at a total drug concentration of 100 mcg/ml and protected from light to prevent degradation. Fifty microliters of each drug sample was injected on the HPLC through the fixed loop injector. Drug concentration was determined by measurement of peak height.

RESULTS AND DISCUSSION

Figure 1 shows a recorder tracing of haloperidol under the conditions described in the methods section.

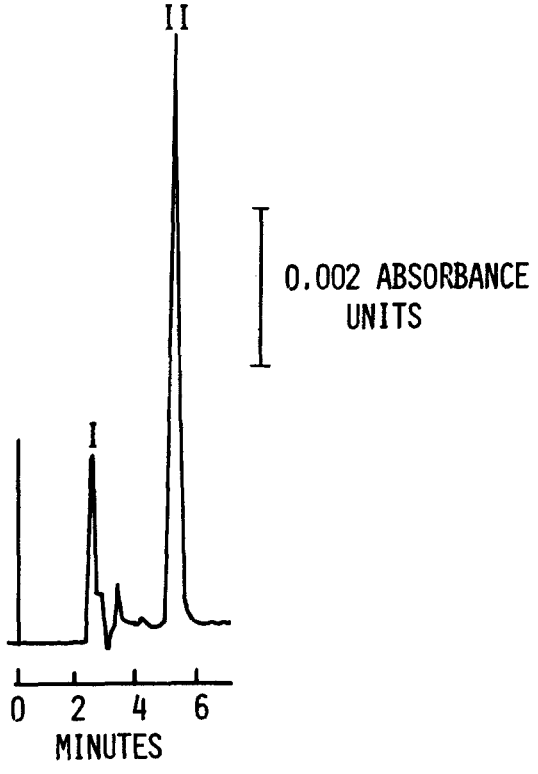

FIGURE 1

The retention time of haloperidol was 5.5 minutes. Several unidentified minor degradation products or contaminants are evident in this tracing. These peaks were not present in freshly prepared drug samples; they were evident only in samples exposed to light for an extended period of time.

The assay is extremely sensitive, a standard curve generated using the height of the haloperidol peak as a function of drug concentration was linear in the range of 50 ng/ml to 1000 ng/ml. Using suitable extraction techniques, this assay could be used for measurement of drug levels in biological fluids.

CONCLUSIONS

A simple, rapid high pressure liquid chromatographic assay for haloperidol in aqueous solutions has been developed. Separation of interfering compounds followed by UV detection at 254 nm allows quantitation of haloperidol concentrations as low as 50 ng/ml. This assay is easier to perform and more sensitive than the current USP XIX assay for this compound.

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REFERENCES

1. "The United States Pharmacopeia", 19th Revision, Mack Publishing Company, Easton, PA, 1975.