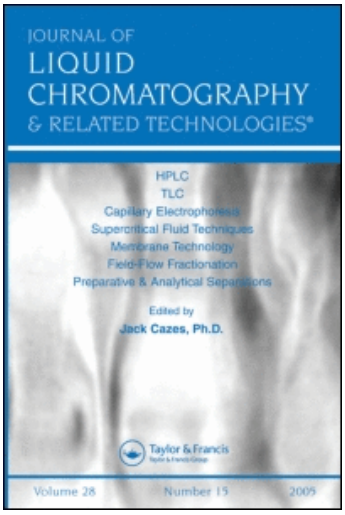

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Determination of Naloxone Hydrochloride in Dosage form by High-Performance Liquid Chromatography

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DETERMINATION OF NALOXONE HYDROCHLORIDE IN DOSAGE FORM BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

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KEY WORDS

High-performance liquid chromatography. Naloxone, determination of.

ABSTRACT

A new, sensitive and rapid method for the determination of naloxone hydrochloride as drug in dosage entity and form using HPLC has been developed. Authentic naloxone hydrochloride was used to establish a calibration curve. A linear relationship was obtained for concentrations ranging from 10 µg/ml to 50 µg/ml. The column used was C_{18}, Micropak MCH-10 (monomeric) and the mobile phase was acetonitrile : 0.01 M KH_2PO_4 (70 : 30) at a flow rate of 2 ml/min. Retention time for naloxone hydrochloride was 3.3 minutes. The proposed method has been proved accurate and precise compared to other pharmacopoeia methods of assay for naloxone hydrochloride.

INTRODUCTION

Naloxone (17-Allyl-4,5-expoxy-3, 14-dihydroxy-morphinan-6-one) is a specific antagonist of pentazocine having a similar action to that of nalorphine but with greater potency.

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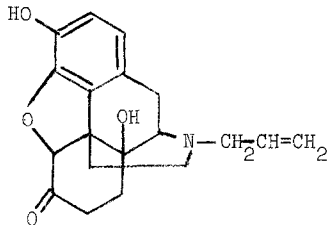

Naloxone hydrochloride is official in the USP XIX[1] where it is assayed by a non-aqueous titrimetric method using standard $HClO_4$ after the addition of mercuric acetate. An injectable solution is also official in the same pharmacopoeia but it is assayed by gas liquid chromatography.

A radioimmunoassay for naloxone in either serum or brain[2] has been developed and several procedures for the gas liquid chromatographic determination of naloxone hydrochloride and naloxone in biological fluids have been reported (3-7).

Thin layer chromatographic techniques, for the identification of the drug in studies of drug abuse using a urine screening program has been developed by Kaistha[8].

Baker[9] and co-workers have characterised several drugs of forensic interest, including naloxone, using hplc reversed phase and normal phase systems whereby the drugs, were identified by their relative retention times and by the ratios of their absorbances at 254 and 280 nm.

The present work describes a rapid, accurate and precise method for the assay of naloxone hydrochloride in dosage form using high-performance liquid chromatography.

EXPERIMENTAL

Apparatus

The HPLC unit is a Varian 8500 LC. Accessory units attached to the instrument are computer model CDS 111, autosampler model

TABLE (1)

The Optimum Values for the HPLC Parameters

Volume injected	:	10 µl
Detector	:	VAR, CHROM, 254 nm, 0.10 AUFS
Flow rate	:	2 ml/min.
Column	:	Commercially available stainless steel (4.0 mm id X 30 cm) packed with C_{18}, micropak MCH - 10 (monomeric).
Eluent	:	70/30 (acetonitrile/0.01 M K H_2PO_4)

8000 and a recorder model 9176. The optimum values for the HPLC parameters established are presented in Table (1).

Non-aqueous potentiometric titrations were performed using a combined glass-calomel electrode assembly and an automatic potentiograph model E576, Metrohm, Herisau, Switzerland.

MATERIALS

Authentic naloxone hydochloride USP[1] was used as obtained without further purification. Water used was doubly distilled in an all-glass still. Acetonitrile was spectral grade Fluka AG.; and all other reagents were analytical grade.

Glacial acetic acid and potassium hydrogen phthalate used for the non-aqueous potentiometric experiments were products of BDH and analytical grade. Mercuric acetate and perchloric acid employed were products of Riedel-De Haen AG., Seezle, Hannover.

METHODS

(1) Determination of Naloxone Hydrochloride by Non-Aqueous Potentiometry:

About 150 mg of authentic naloxone hydrochloride was accurately weighed and dissolved in a mixture of 20 ml glacial acetic acid and 5 ml of mercuric acetate (5% w/v). The potentiometric titration curve was recorded using the potentiograph and the end point of the titration was estimated by the method of parallel tangents (10). The percentage of naloxone hydrochloride was computed from the following expression:

$$\text{Percentage of Naloxone Hydrochloride} = \frac{V \times F \times 36.38}{\text{weight of naloxone hydrochloride sample}} \times 100$$

where V and F are the volume (in millilitres) and factor for the standard (0.1 N) acetous perchloric acid respectively, and 36.38 is the number of milligrams of naloxone hydrochloride chemically equivalent to 0.1 N - perchloric acid.

The calculated percentage of naloxone hydrochloride was used for correction of concentrations employed in the establishment of the calibration curve.

(2) Preparation of Standard Curve:

A stock solution containing 50 mg of naloxone hydrochloride per 100 ml of the eluent solution was prepared, and serial dilutions were made in the same vehicle to give solutions containing 0.1, 0.15, 0.2, 0.25, 0.3, 0.4 and 0.5 mg per 10 ml. Triplicate injections of 10 μl each were made onto the column. The integrator count was plotted versus concentration of naloxone hydrochloride.

(3) Determination of Naloxone Hydrochloride in Dosage Form:

Naloxone hydrochloride is available commercially as an injectable

Peak No. 1 – Solvent peak

Peak No. 2 – Naloxone Hydrochloride (Retention time–3.3 min)

Fig. 1

(Narcan$^{(R)}$, neonatal) labelled to contain 0.02 mg per ml of naloxone hydrochloride in addition to 0.86% sodium chloride and 0.2% of 9:1 mixture of methyl to propylparaben.

Six ampoules were randomly sampled. Triplicate injections of 10μl each were withdrawn from each ampoule and made onto the column. Using the average integrator count, the concentration of naloxone hydrochloride was determined from the standard curve. Similarly added recovery experiments were carried out by spiking the ampoule contents with known amounts of authentic naloxone hydrochloride.

RESULTS AND DISCUSSION

Fig. 1 shows a tracing of a typical chromatogram obtained by HPLC. Under the conditions described above, the retention time was 3.3 min.

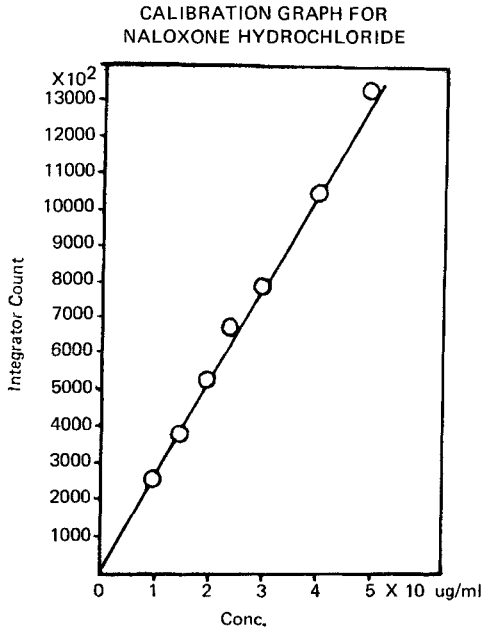

Fig. 2

Fig. 2 shows the relationship between the concentration of naloxone hydrochloride and the integrator count. A straight line is obtained demonstrating the applicability of this procedure for assaying naloxone hydrochloride in concentration range 10μg/ml to 50μg/ml. Furthermore the results of applying the new HPLC method to the determination of naloxone hydrochloride in its dosage form (Narcan(R), Neonatal) of injections are shown in Table 2. The results of spiking shown in Table (2) indicate a percentage recovery of 99.0 ± 2.6. It can be concluded that the HPLC method described here for the determination of

(R) Endo Laboratories, Inc.
Subsidiary of EI. du Pont de Nemours & Co
Garden City N.Y. 11530.

TABLE (2)

High Performance Liquid Chromatographic Determination of Naloxone Hydrochloride and in Dosage Form.

Sample	Stated amount of Naloxone hydrochloride µg/ml	Added amount µg/ml	Percentage recovery*	Standard deviations
Authentic Naloxone hydrochloride.	15	-	98.0	± 2.4
Narcan Neonatal injectable (R).	20	-	97.1	± 2.8
	20	19.98	99.0	± 2.6

*Mean of six runs.

naloxone hydrochloride in bulk and in its dosage form is rapid, accurate and simple to perform.

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