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Note

High-performance liquid chromatographic determination of loperamide hydrochloride in pharmaceutical preparations

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Loperamide is an antidiarrhoeal used for the symptomatic relief of diarrhoeas not controlled by absorbent mixtures. Its hydrochloride salt and the capsule formulation are monographed in the *United States Pharmacopoeia* (USP)[1]. Other formulations of loperamide hydrochloride include tablets and syrups.

The method adopted in ref. 1 for the assay of loperamide hydrochloride capsules involves chloroform extraction, followed by the formation of a coloured complex with the indicator Tropaeolin OO and the measurement of colour intensity in toluene. This procedure, however, was found not to be applicable to syrup preparations because polyhydric alcohols such as propylene glycol, which are commonly added to syrups to retard the crystallization of sugar, would interfere with the colour formation. There are few other reports on the assay of loperamide in pharmaceutical preparations.

This paper reports a high-performance liquid chromatographic (HPLC) procedure using an adsorption column for the determination of loperamide in different pharmaceutical dosage forms. The method is rapid and simple and is free from interference from common excipients. Its reliability is demonstrated by comparing results with the official assay method and recovery tests.

EXPERIMENTAL

Chromatographic conditions

A modular system comprised of a Perkin-Elmer Series 10 pump, a Rheodyne 7125 injector with a 50-μl loop, a Perkin-Elmer LC-15B fixed-wavelength (254 nm) detector and a Shimadzu C-R3A recording integrator was employed. A 25 cm × 4.6 mm Perkin-Elmer Analytical 10-μm silica column was used. The mobile phase was chloroform–methanol–ammonia (95.5:4.5:0.05), the flow-rate was 2 ml/min and the detector sensitivity setting was 0.016 a.u.f.s.

Stock standard solution

About 10 mg of loperamide hydrochloride were accurately weighed and dissolved in 100 ml of chloroform.

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Internal standard solution

A 10-mg amount of cyclizine hydrochloride was dissolved in 25 ml of chloroform.

Working standard solutions

To three 25-ml volumetric flasks each containing 1.0 ml of internal standard solution, were added respectively 5, 10 and 15 ml of the stock standard solution and made up to the mark with chloroform. These working standard solutions contain respectively 0.02, 0.04 and 0.06 mg/ml of loperamide hydrochloride.

Procedure

Capsules and tablets. An accurately weighed quantity of a powdered mixture obtained from 20 capsules or tablets equivalent to about 10 mg of loperamide hydrochloride was transferred to 1 100-ml volumetric flask and about 80 ml of chloroform were added. The flask was shaken for about15 min and then made up to the mark with chloroform. The solution was quickly filtered through a covered filter, discarding the first 10–20 ml of the filtrate, and collecting the remainder in a glass-stoppered flask. A 5-ml volume of this solution was pipetted into a 25-ml volumetric flask, 1.0 ml of internal standard solution was added, followed by mixing and making up to the mark with chloroform. This solution was injected for HPLC using a microsyringe. The peak area ratio of loperamide hydrochloride to the internal standard was measured and the content calculated with reference to a calibration graph prepared from the working standard solutions.

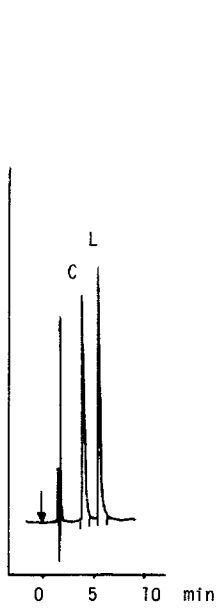
Syrup. A quantity of sample equivalent to about 10 mg of loperamide hydrochloride was transferred to a separating funnel containing 30 ml of distilled water. The contents were extracted with four 20-ml portions of chloroform, filtering each portion through a pledget of glass wool into a 100-ml volumetric flask. After mixing and making up to the mark with chloroform, 5 ml of this solution were pipetted into a 25-ml volumetric flask. The above procedure was then employed.

RESULTS AND DISCUSSION

When the HPLC procedure was first developed, the more commonly used reversed-phase separation was attempted. As in the case of other common basic drugs, base modifiers or ion-pair agents were used to improve the elution pattern and peak shape. However, for loperamide hydrochloride, common ion-pair agents such as hexanesulphonate and octanesulphonate were found to be of little use in improving the elution time and peak symmetry.

The procedure was repeated using an adsorption column. A 10-μm silica column together with the mobile phase chloroform–methanol–ammonia (95.5:4.5:0.05) were found to give good separation of loperamide and the chromatographic peak could be used for quantitation. To improve the repeatability, the internal standard cyclizine hydrochloride was used throughout for peak area ratio measurements. A typical chromatogram of loperamide and the internal standard is shown in Fig. 1.

A UV detector was used for the detection of loperamide. The UV absorption maxima were in the region of 250–280 nm as shown in Fig. 2. For simplicity, a fixed wavelength (254 nm) detector was employed.



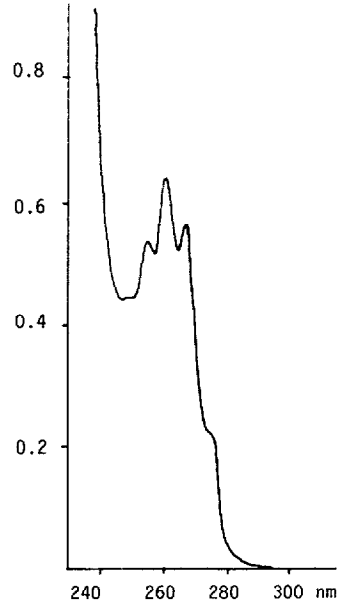


Fig. 1. Chromatogram of loperamide hydrochloride (L) and the internal standard cyclizine hydrochloride (C). See text for chromatographic conditions.

Fig. 2. Absorption spectrum of 0.05% loperamide hydrochloride in methanol (1-cm cell).

The working range of standard solutions of loperamide hydrochloride used for the preparation of the calibration graph was 0.02–0.08 mg/ml and the graph was found to be linear. The sample solutions were adjusted to similar concentrations for the determination of the loperamide hydrochloride content.

The results of the analysis of three commercial preparations of loperamide hydrochloride using both the HPLC procedure proposed and the USP colorimetric method was shown in Table I. For capsules and tablets, the results obtained by both methods were close and comparable. For syrup, the results obtained by the official method were much higher. Subsequent investigations revealed that this sample contained small amounts of propylene glycol which was partly extracted into

TABLE I

DETERMINATION OF LOPERAMIDE HYDROCHLORIDE IN PHARMACEUTICAL PREPARATIONS

Preparation	*Content claimed*	*Percentage of labelled content found*	
		*HPLC method**	*USP method*
Capsule	2 mg	96.1 (±0.9)	96.7
Tablet	2 mg	96.5 (±1.1)	97.2
Syrup	2 mg/ml	102.3 (±1.3)	122.5

* Mean of three determinations, with the standard deviation in parentheses.

chloroform together with loperamide hydrochloride. This polyhydric alcohol was found to impart a yellow colour to the final toluene layer, rendering the USP method not directly applicable to this syrup preparation. The HPLC method proposed, however, was free from interference from this excipient.

To validate further the reliability of the proposed procedure, two synthetic mixtures containing known amounts of loperamide hydrochloride were prepared. The first one was a mixture containing lactose which is a common ingredient in capsules and tablets. The second one was a mixture containing syrup and small amounts of chloroform spirit and propylene glycol. The recovery from these two mixtures was found to be 99.5 $\pm$ 0.7 and 99.2 $\pm$ 1.0% respectively, indicating the applicability of the HPLC procedure to both solid and liquid formulations of loperamide hydrochloride.

ACKNOWLEDGEMENT

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REFERENCE

1 *United States Pharmacopeia*, Mack Publishing Company, Easton, PA, 21st revision, 1985, p. 604.