Journal of Chromatography, 178 (1979) 579–582
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CHROM. 12,138

Note

High-performance liquid chromatographic analysis of lidocaine hydrochloride formulations

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(First received May 22nd, 1979; revised manuscript received June 18th, 1979)

Lidocaine (lignocaine) hydrochloride is a local anaesthetic widely used for injections and for local application to mucous membranes. Injections are normally of strengths ranging from 0.5 to 2.0% (w/v), either formulated with lidocaine hydrochloride alone or with the sympathomimetic epinephrine or norepinephrine. One common preparation for local application is lidocaine gel which normally contains 2.0% (w/v) of lidocaine hydrochloride. These formulations usually contain preservatives or bactericides such as chlorocresol, cresol and esters of hydroxybenzoic acid.

The official methods of analysis for lidocaine hydrochloride involve non-aqueous titration with perchloric acid[1], acide–base titration of the extracted base[2] and titration with sodium dioctyl sulphosuccinate[3]. Other methods of determination rely on colour formation with bromocresol green[4] and gas–liquid chromatography[5–9]. In general, most of these methods work well for the common preparations containing lidocaine hydrochloride, although some require preliminary sample treatment such as solvent extraction and others are non-specific and relatively time-consuming.

High-performance liquid chromatography (HPLC) has been used in the separation of lidocaine in plasma[10] and in one formulation[11], using adsorption columns. During investigations into possible applications of HPLC in the analysis of pharmaceutical preparations, it was found that lidocaine hydrochloride in injections and gels could be determined by a simple HPLC procedure, using a reversed-phase column. The method requires simple sample preparation, is rapid and specific and there is no interference from the common co-existing active ingredients and preservatives or bactericides. The results obtained by the proposed method compared closely with those obtained using the official titrimetric procedures.

For a 2% lidocaine hydrochloride injection containing 0.1% of chlorocresol, simultaneous determination of both compounds can be made by slightly modifying the operating conditions.

EXPERIMENTAL

Apparatus

An Altex HPLC system was used, consisting of a Model 100A pump capable of operating at an inlet pressure up to 10,000 p.s.i., a 20-μl constant-volume

loop injector, a LiChrosorb C_2 10-μm microparticulate reversed-phase column (250 × 3.2 mm I.D.) and a Model 155 variable-wavelength detector (used with a Hitachi Model 100-30 spectrophotometer) set at wavelength 263 nm. The chromatograms were recorded on a Rikadenki Model B-28H recorder, with full-scale range set at 10 mV.

Chromatographic conditions

The eluting solvent was a 1:1 mixture (pH 7.90) of distilled methanol and 0.1% of dibasic ammonium phosphate in distilled water. Column temperature was ambient. Flow-rate of the eluting solvent was set at 1.5 ml/min (inlet pressure *ca.* 2700 p.s.i.). Injection of solution to the 20-μl loop was made by a microsyringe. A full scale absorbance unit of 0.1 was used. Chart speed of the recorder was set at 15 cm/h.

Preparation of standard and sample solutions

Standard. A set of standard aqueous solutions was prepared to contain 0.5–1.5 mg/ml of lidocaine hydrochloride.

Sample. For injections, a measured volume of sample was diluted with water to a concentration of 1 mg/ml of lidocaine hydrochloride. For water-miscible gel with lidocaine hydrochloride content expressed in terms of per cent (w/v), similar dilution was made on a weighed aliquot, and the final calculation was based on the density which was determined by weighing a measured volume of the gel.

RESULTS AND DISCUSSION

Lidocaine hydrochloride was separated by the C_2 reversed-phase column using a slightly alkaline eluting solvent. Although strongly basic solutions are not usually recommended for bonded phase packing materials, the proposed mildly alkaline medium did not affect the column, especially when the latter was thoroughly flushed with distilled water and methanol after use.

Detection of lidocaine hydrochloride was made at the maximum UV absorption at 263 nm. For instruments with a fixed wavelength detector, detection at 254 nm may also be used.

Three samples were analyzed by the proposed procedure and by the official methods laid down in British Pharmacopoeia (B.P.) and British Pharmaceutical Codex (B.P.C.): sample 1, injection containing 2% of lidocaine hydrochloride and 0.1% of chlorocresol; sample 2, injection containing 2% of lidocaine hydrochloride, 0.005% of 1-norepinephrine with methyl hydroxybenzoate and propyl hydroxybenzoate as preservatives; sample 3, water-miscible gel containing 2% of lidocaine hydrochloride with methyl hydroxybenzoate, propyl hydroxybenzoate and *m*-cresol as preservatives.

Chromatograms of a standard solution and solutions from the above samples are shown in Fig. 1.

Quantitative determinations were carried out by measuring the peak height of lidocaine hydrochloride sample solutions and comparing with a calibration graph obtained using the prepared standards. The graph was found to be linear throughout the concentration range 0.5–1.5 mg/ml lidocaine hydrochloride. Results of analysis

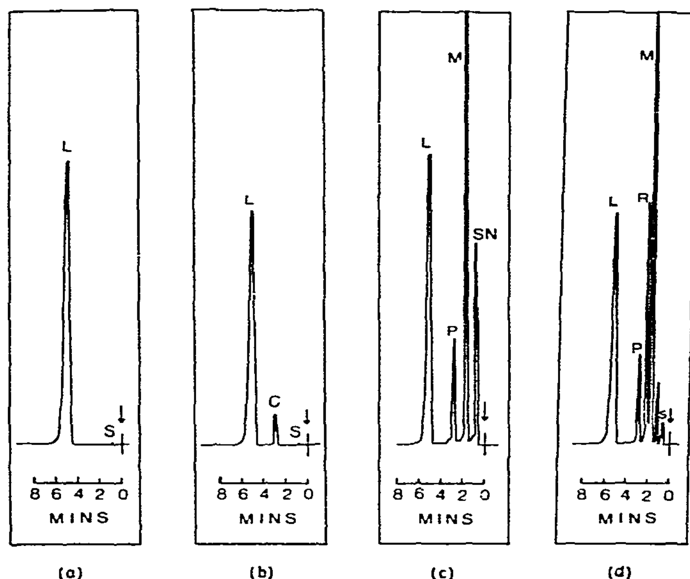

Fig. 1. Chromatograms of lidocaine hydrochloride. (a) Standard solution; (b) sample 1; (c) sample 2; (d) sample 3. Peaks: S = solvent; L = lidocaine hydrochloride; C = chlorocresol; SN = solvent and l-norepinephrine; M = methyl hydroxybenzoate; P = propyl hydroxybenzoate; R = *m*-cresol.

are shown in Table I from which it can be seen that the HPLC results are in close agreement with those obtained using the official titrimetric procedures.

The reproducibility of the 20-μl constant-volume loop injection was checked by making ten consecutive injections of the same solution and measuring the peak heights obtained. The relative standard deviation was found to be less than 2.0%.

TABLE I

ANALYSIS OF LIDOCAINE HYDROCHLORIDE IN FORMULATIONS

Labelled content of lidocaine hydrochloride was 2.0% w/v in each case.

Sample	*Percentage of labelled content found*	
	*HPLC method**	*Official method*
1 Injection	98.1 ± 1.5	97.7 (B.P.)
2 Injection	102.3 ± 1.8	101.1 (B.P.)
3 Gel	101.7 ± 2.6	103.0 (B.P.C.)

* Mean of five determinations with the standard deviation.

For the sample injection containing 2% of lidocaine hydrochloride and 0.1% of chlorocresol, simultaneous determinations of both compounds were made by using the same chromatographic conditions but with the detection wavelength set at 273 nm at which the peak height of chlorocresol was comparable to that of lidocaine hydrochloride. Chrlorocresol was then determined by refering to a calibration graph obtained by using a set of standard aqueous solutions containing 0.02–0.08 mg/ml of chlorocresol. Results from one determination of chlorocresol in sample 1

were found to be 96.6% of the labelled content compared with 94.4% obtained by colorimetric determination with 4-aminophenazone[12]. The chromatograms for this determination are shown in Fig. 2.

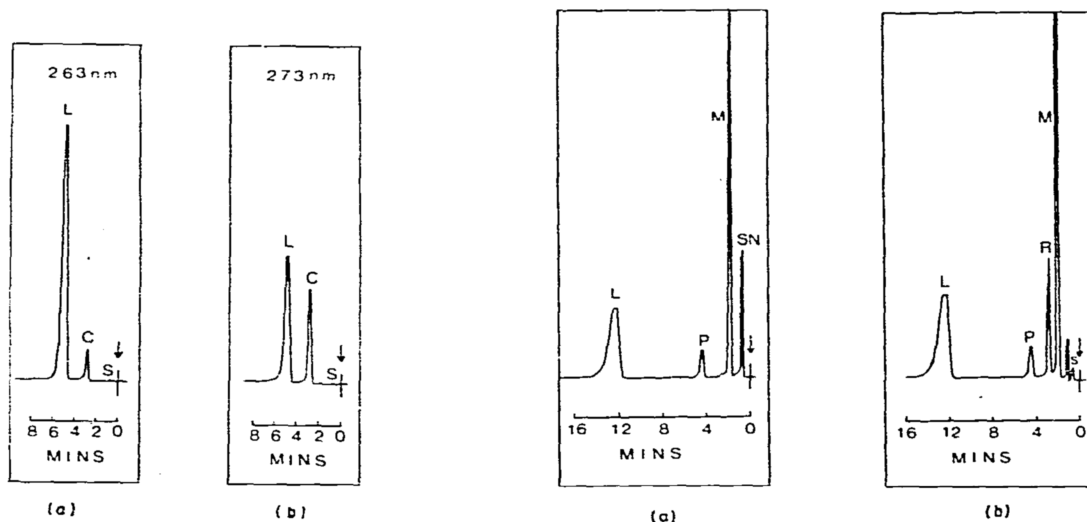

Fig. 2. Chromatograms of solution from sample containing 2% of lidocaine hydrochloride and 0.1% of chlorocresol. Detection at 263 nm (a) and 273 nm (b). Peak designations as in Fig. 1.

Fig. 3. Separation of preservatives from lidocaine hydrochloride. (a) Sample 3 (*cf.* Fig. 1c); (b) sample 4 (*cf.* Fig. 1d). Peak designations as in Fig. 1.

A better separation of other preservatives in the other two samples was achieved using an eluting solvent consisting of a 40:60 mixture of methanol and 0.1% dibasic ammonium phosphate. Chromatograms are shown in Fig. 3.

ACKNOWLEDGEMENT

The author thanks Dr. A. J. Nutten, Government Chemist of Hong Kong, for the permission to publish this paper.

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