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Determination of lidocaine in pharmaceutical preparations using thin-layer chromatographic densitometry*

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Abstract: A thin-layer chromatographic (TLC)–UV-densitometric method has been developed for the analysis of lidocaine in ointments, suppositories and gels. The method is quantitative, rapid and able to separate lidocaine from other components in the pharmaceutical dosage forms investigated without preliminary extraction. The method gave precise and reproducible results.

Keywords: *Lidocaine formulations; thin-layer chromatographic densitometry.*

Introduction

Lidocaine (2-diethylaminoaceto-2′,6′-xylidide) is widely used with other drugs in pharmaceutical preparations as a local anaesthetic. The determination of lidocaine in ointments, suppositories and gels containing corticosteroids, polyhydric alcohols and methyl or propyl esters of *p*-hydroxybenzoic acid is often required.

Various methods have been reported for the determination of lidocaine in pharmaceutical preparations including the spectrofluorimetric methods which are applied after the extraction of an ion-pair of lidocaine with aluminium (III) ion [1], cobalt-thyocianate [2], bromocresol-green [3] or bromophenol-blue [4]. Gas–liquid chromatography (GLC) has been used after extraction of the lidocaine from pharmaceutical preparations [5]. In recent years high-performance thin-layer chromatography (HPTLC) has also been used for the quantitative analyses of lidocaine in samples which contain other local anaesthetic drugs [6–8].

The aim of this work was to determine lidocaine in pharmaceutical preparations which contain active principles other than local anaesthetics. The proposed UV-densitometric method enables a direct determination of lidocaine from the thin-layer plates without prior elution and represents a simple and easily reproducible procedure which could be applied to the analysis of lidocaine in ointments, suppositories and gels.

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Experimental

Materials

Lidocaine, acetone, di-isopropylether, diethylamine, ethanol and silica gell GF_{254} plates were obtained from Merck (Darmstadt, FRG). "Doxafen Plus" suppositories and ointment were obtained from Ljek (Ljubljana, Yugoslavia). "Xyloproct" suppositories and ointment, and "Xylocain" gel and ointment were obtained from Bosnaljek (Sarajevo, Yugoslavia). The content of lidocaine in these pharmaceutical dosage forms can be seen in Table 1.

Equipment

UV-densitometric analyses were performed with HPTL SCANNER Camag (Muttenz, Switzerland). The solutions were applied with a Linomat III Camag (Muttenz, Switzerland).

Chromatographic conditions

The standard solutions of lidocaine were prepared in absolute ethanol and a calibration curve prepared with eight standard solutions having concentrations of 10–80 μg/10 μl (4.2×10^{-3}–3.4×10^{-2} mol l^{-1}).

The active substances were extracted from pharmaceutical dosage forms with absolute ethanol. One suppository or 1 g of ointment was dissolved in 10 ml of warm absolute ethanol and after cooling down the suspension was placed in a 20-ml glass-stopped centrifuge tube. The layers were separated by centrifugation (5 min at 2000 rpm) and the clear ethanolic layer was transferred to a 25-ml volumetric flask. The residue in the centrifuge tube was extracted with 2 × 5 ml of warm absolute ethanol, the ethanolic layers transferred to the same volumetric flask, and made up to volume with absolute ethanol. For gels, 1 ml was placed in a 10 ml volumetric flask made up to volume with absolute ethanol. The ethanolic extracts were applied to the chromatographic plates. Other conditions are given in Table 1.

For the isolation of lidocaine from other active principles, chromatographic plates (20 × 20 cm) coated with silica gel GF_{25}d24 layer of 0.25 mm thickness, were used. The mobile phase was di-isopropylether–acetone–diethylamine (85:10:5%, v/v/v). Spots were detected under UV light at 254 nm.

Table 1
Conditions of the determination of lidocaine from pharmaceutical preparations

Sample	Content of lidocaine per dry g	Solution of lidocaine in methanol mg ml^{-1}	Conc. of the standard and sample in methanol mol l^{-1}	Taken μl	Taken μg
"Xyloproct" suppositories	60 mg l^{-1} sup.	60 mg 25 ml^{-1}	10^{-2}	20	48
"Xyloproct" ointment	50 mg lg^{-1}	50 mg 25 ml^{-1}	8.5×10^{-3}	20	40
"Xylocain" ointment	50 mg lg^{-1}	50 mg 25 ml^{-1}	8.5×10^{-3}	20	40
"Xylocain" gel	20 mg ml^{-1}	20 mg 10 ml^{-1}	8.5×10^{-3}	20	40
"Doxafen Plus" suppositories	40 mg l^{-1} sup.	40 mg 25 ml^{-1}	6.8×10^{-3}	25	40
"Doxafen Plus" ointment	20 mg lg^{-1}	20 mg 25 ml^{-1}	3.4×10^{-3}	50	40

UV-densitometric determination

The measurements were performed on a HPTL scanner, readings being taken directly from the thin-layer. The content of lidocaine was calculated according to the equation:

$$K_a = P_a K_{STD}/P_{STD}$$

where K_a is the amount of active substance, P_a is the peak area of active substance, K_{STD} is the amount of the standard and P_{STD} is the peak area of the standard.

Results and Discussion

By using a UV-densitometric method coupled with thin-layer chromatograpy it is possible to separate lidocaine from other components without performing an extraction, and determine it by direct reading from the thin-layer plate thus avoiding elution of the spot.

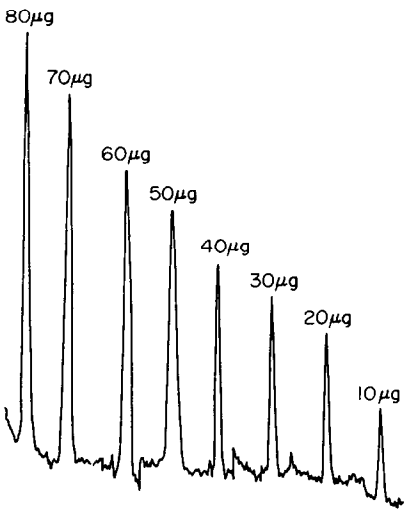
The UV-densitometric method was developed using standard substances and then was applied to suppositories, gels and ointments.

Ethanol was found to be the best solvent for extraction. Conditions for measurements on the HPTL scanner were established experimentally: wave length 254 nm, selection of the slit width 2 mm (micro position) speed 2 mm s^{-1}, mode selector linear measure and scanning parameters $A = 1$ cm, $B = 2$ cm. Calibration densitograms, such as Fig. 1, were prepared in triplicate and the mean values used for the lidocaine calibration.

Over the concentration range of 10–80 μg/10 μl, linear regression analysis of lidocaine peak area versus lidocaine concentration ($N = 8$) yielded an equation $yx = 0.04816x - 0.0820$ ($r = 0.9998$).

These conditions were employed to determine the recovery of lidocaine from some pharmaceutical formulations, and Table 2 shows that recoveries were in the range of 99.2–100.7%. Results obtained by peak height were almost identical to those obtained using peak area.

The precision of the assay was determined by 20 analyses of a single sample of a drug



UV – Densitogram of lidocaine

Figure 1

Table 2
Recovery of lidocaine from pharmaceutical preparations

Sample (N = 20)	Taken μg	Peak area Found μg	SD μg	R %	Peak height Found μg	SD μg	R %	$P > 0.05$
"Xyloproct" suppositories	48	48.2	0.883	100.4	48.1	0.876	100.2	$P > 0.1$
"Xyloproct" ointment	40	39.9	0.797	99.7	39.8	0.801	99.5	$P > 0.3$
"Xylocain" ointment	40	39.8	0.682	99.5	39.7	0.881	99.2	$P > 0.3$
"Xylocain" gel	40	40.2	0.222	100.4	40.3	0.231	100.7	$P > 0.5$
"Doxafen Plus" suppositories	40	40.1	0.851	100.4	39.9	0.846	100.2	$P > 0.1$
"Doxafen Plus" ointment	40	39.8	0.692	99.5	40.0	0.685	100.0	$P > 0.3$

SD = standard deviation.
R = recovery.

Table 3
Precision of assay for lidocaine

Sample	Mean lidocaine concentration in methanol	Rel. std. dev. (RSD) Peak area %	Peak height %
"Xyloproct" suppositories	2.4 mg ml^{-1}	1.83	1.82
"Xyloproct" ointment	2 mg ml^{-1}	2.00	2.01
"Xylocain" ointment	2 mg ml^{-1}	1.71	2.22
"Xylocain" gel	2 mg ml^{-1}	0.55	0.57
"Doxafen Plus" suppositories	1.6 mg ml^{-1}	2.12	2.12
"Doxafen Plus" ointment	0.8 mg ml^{-1}	1.74	1.71

formulation. The relative standard deviations were less than 3.0%, for all the formulations, as shown in Table 3.

The excellent recovery and precision obtained by this procedure indicate that it is very suitable for the determination of lidocaine in the formulations examined.

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