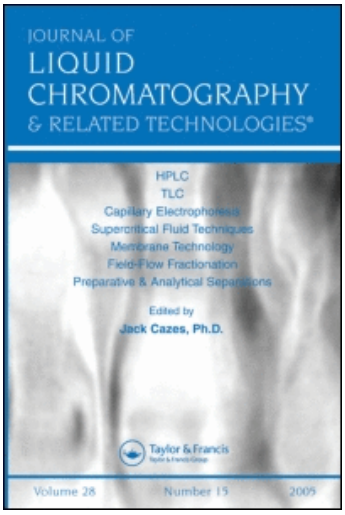

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Analysis of Dexamethasone Acetate in Pharmaceutical Formulations by HPLC

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ANALYSIS OF DEXAMETHASONE ACETATE IN PHARMACEUTICAL FORMULATIONS BY HPLC

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ABSTRACT

A rapid and effective high-pressure liquid chromatographic method has been developed for the quantitative determination of dexamethasone 21 acetate in pharmaceutical formulations.Sample preparation employs a simple extraction procedure and analysis is carried out on a reverse-phase chromatographic system using a LiChrosorb RP 18 column and a water-acetonitrile as mobile phase.The extraction procedure gives quantitative recovery and chromatographic results show that drug levels of as 0.1 ppm can be conveniently analyzed without significant background interferences.

INTRODUCTION

The action,uses and side effect of dexamethasone 21 acetate are those of dexamethasone,a syntetic adrenal steroid derived from prednisolone.Dexamethasone acetate is particularly employed as a repository form of dexamethasone,for systemic or intralesional use.

Current analytical techniques for quantitative dexamethasone

determination in various biological and non biological media are based on colorimetric methods with bleu tetrazolium or with a modified Oorter-Silber reagent (1).Problems associated with the analyses are usually complex;colorimetric methods do not seem sufficiently quantitative when dexamethasone incorporated into a complicated matrix is being analyzed, furthermore they are time consuming for routine work and rather tedious to perform.

High-pressure liquid chromatography (HPLC) has been recently proposed as an alternative procedure for the determination of dexamethasone phosphate sodium salt (2,3).

The present paper is an application of reverse-phase HPLC to routine analyses of dexamethasone acetate in pharmaceutical formulations, in the range of 10 ng level.

MATERIALS AND METHODS

Pharmaceutical formulations (dermal ointments and suppositories) containing dexamethasone acetate,were prepared for chromatographic analyses as follows:

ointments: ointment sample (5 g) exactly weighed were suspended in 100 ml of twice-distilled warm water (40 °C),quantitatively poured into a 250 ml separatory funnel and then extracted with 50 ml of chloroform.The extraction was repeated three times.The lower (chloroform) layers were transferred into a 500 ml separatory funnel and washed twice with 100 ml of redistilled water.The washed extract was filtered through 25 g of anhydrous sodium sulfate (held in 60 ml coarse fritted-glass funnel).The anhydrous

extract was evaporated to dryness under reduced pressure in a rotary evaporator.The residue was redissolved in acetonitrile (LiChrosolv,Merck) filtered through a Gelman Acrodisc-CR 0.45 μm filter and then diluting to volume into a 25 ml volumetric flask;
suppositories: four suppositories (8 g) were dissolved in 100 ml of warm ethanol (40 °C).The clear ethanolic solution was stored overnight in a refrigerator (4 °C).This treatment removes a substantial proportion of inactive lipid suppository base which was subsequently separated by filtration through a Whatman GF/C filter.The filtered solution was evaporated to dryness,redissolved in 100 ml of diethyl ether,transferred into a 500 ml separatory funnel and then extracted twice with 100 ml of redistilled water.This treatment is useful to eliminate the water solubile ingredients.The diethyl ether layer was dried and evaporated to dryness.The residue was redissolved in acetonitrile,filtered and diluting to volume into a 25 ml volumetric flask.

Dexamethasone acetate standard was obtained from commercial suppliers.The stock solution of 0.5 mg/ml was made by dissolving in acetonitrile 5 mg of dexamethasone acetate,exactly weighed on a Cahn electrobalance mod. G 2 and diluting to volume into a 50 ml volumetric flask. An aliquot (5 ml) of the stock solution was accurately measured and transferred into a 50 ml volumetric flask and diluted to volume with acetonitrile.Injections of 10 μl of dexamethasone acetate standard solution (0.11 μg/μl) were made for quantitation.

The chromatographic separations were performed with a Perkin-Elmer Series 3B liquid chromatograph.Component elution was monitored with a LC-75 variable wavelength detector (190-600 nm) equipped with a LC-75

Autocontrol.The column was a Hibar-LiChrosorb RP 18 10 µm (Merck, 25 x 0.26 cm I.D.).The separations reported were achieved under the following conditions: mobile phase,50% acetonitrile (LiChrosolv,Merck) in deionized redistilled water;flow rate,1.5 ml/min;temperature,25 °C; wavelength,238 nm;chart speed,0.5 cm/min.Graphs were generally obtained with an attenuation setting corresponding to 0.16 AUFS on a 10 mV recorder and peak areas were determined by a Perkin-Elmer Sigma 10 integrator.

RESULTS AND DISCUSSION

A chromatogram of ointment extract containing dexamethasone acetate is shown in Figure 1.The dexamethasone acetate peak is completely resolved and is symmetrical.Detector response, as measured from standard peak heights,was linear up to at least 0.1 µg.The minimum detection limit was 10 ng;belowe this level baseline detector noise exceeded peak height.The accuracy of the proposed method was further checked by means of recovery experiments carried out on one rappresentative pharmaceutical preparation (ointment and suppository) in which a measured quantity of dexamethasone acetate was added to the sample.The mean recovery of dexamethasone acetate in dermal ointment was 98% with a relative deviation of ±1.5%, the mean recovery in suppositories was 96% with a relative deviation of ±2%.With the proposed method there was no interference from propyl gallate,butyl hydroxyanisole,tween 80 and other active or inactive ingredients present in ointment and suppositories.

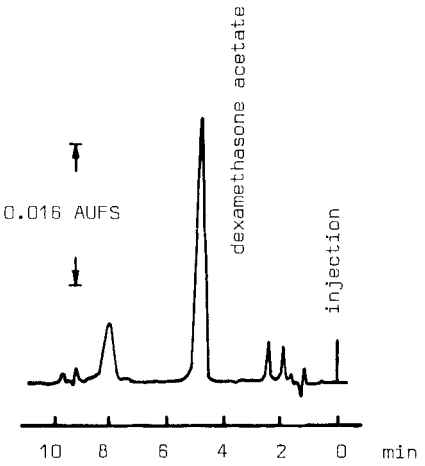

Figure 1

HPLC chromatogram of an acetonitrile extract (10 µl) of a dermal ointment sample containing dexamethasone acetate.Conditions:column,LiChrosorb RP 18 10 µm (Merck,25 x 0.26 cm I.D.);mobile phase,water-acetonitrile (1:1);flow rate,1.5 ml/min;temperature,25 OC;chart speed,0.5 cm/min;wavelength,238 nm.

CONCLUSION

The proposed method for the assay of dexamethasone acetate in pharmaceutical formulations confirms that the HPLC technique has several distinct advantages over the conventional technique currently in use.It is simple,fast and has a precision and accurancy greater than those of the more tedious colorimetric methods.We believe that the technique described here can be used,with a slight modification of the extraction procedure,for measured dexamethasone acetate,in other pharmaceutical formulations,in biological materials (plasma) and for analysing samples where interference is too great for the use of other techniques.

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