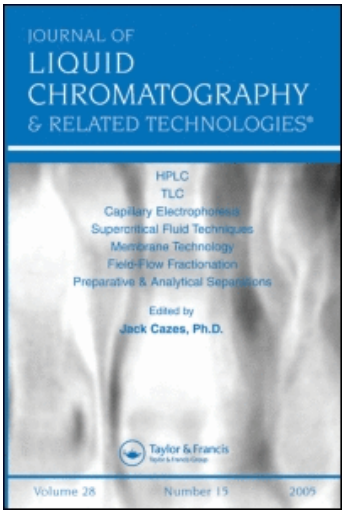

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Anti-Hormonal Agents: 3. HPLC of Cyproterone Acetate

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ANTI-HORMONAL AGENTS. III. HPLC OF CYPROTERONE ACETATE

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ABSTRACT

A procedure is described for the reverse phase HPLC analysis of the anti-androgenic steroid cyproterone acetate in tablets containing 5 and 10 mg dosages. Samples of these tablets stored for more than 10 years showed no sign of deterioration.

INTRODUCTION

We have a recently described suitable methods for the HPLC analysis of the anti-hormonal steroids RU 38486 [1] and ZK98734 [2], which exhibit anti-glucocorticoid and anti-progestational activities. The latter property makes these steroids of interest as potential contraceptive agents for women. At present, there is no widely accepted hormonal contraceptive agent for men, but the anti-androgenic steroid cyproterone acetate (Figure 1) is known to suppress spermatogenisis and some clinical studies have been reported [3-6]. In addition, cyproterone acetate finds clinical applications in the management of certain forms of prostatic cancer, acne, hirsutism and precocious puberty [7-10]. Cyproterone acetate is most

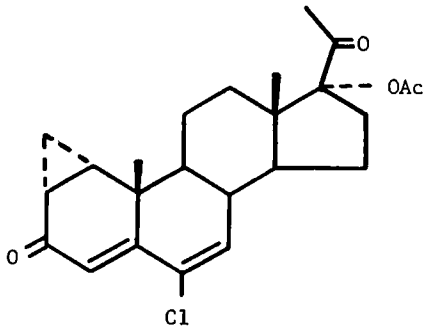

Figure 1 **Cyproterone acetate**

commonly administered in tablet form, but hitherto there have been no reports of the analysis of the tablet formulation.

In this paper we present details of a suitable method for the HPLC analysis of cyproterone acetate in tablet formulations at two dose levels. Application of the method to tablets which had been stored for more than ten years indicates a very long shelf life for these formulations.

EXPERIMENTAL

Cyproterone acetate standard was purified by preparative TLC on Merck silica GF254, eluted with MeCN:CH_2Cl_2 85:15 v/v.

Tablets of cyproterone acetate containing declared doses of 5 and 10 mg respectively were manufactured by Schering AG, Berlin.

Each tablet was extracted by grinding to a powder and adding 20.0 ml MeOH, the mixture being agitated in an ultrasonic bath for 10 min. Insoluble excipients were spun down on a centrifuge and the supernatant transferred to a capped vial for storage. Standard solutions of pure cyproterone acetate in MeOH were used for calibration of the HPLC.

General methods and procedures for the analytical HPLC have been described previously [1-2]. Analyses

TABLE 1

Analysis of cyproterone acetate content of tablets

Tablet No.	weight mg	content mg/tablet	% of declared
5 mg tablets			
1	120.0	4.96	99.2
2	121.3	5.15	103.7
3	118.4	4.96	99.2
4	118.1	4.89	97.9
5	121.2	4.81	96.2
6	122.4	5.20	104.0
7	123.3	5.11	102.3
8	121.8	4.99	99.9
9	120.8	5.02	103.4
10	124.0	5.29	105.7
Average	121.1	5.04	100.8
Range			-3.8% to +5.7%
10 mg tablets			
1	123.5	10.31	103.1
2	120.3	9.93	99.3
3	129.1	10.50	105.0
4	122.2	10.18	101.8
5	123.4	10.41	104.1
6	116.8	9.74	97.4
7	121.2	10.18	101.8
8	124.9	10.48	104.8
9	117.0	10.06	100.6
10	118.6	10.16	101.6
Average	121.7	10.16	101.6
Range			-2.6% to +5.0%

were performed on a 25 cm x 4.5 mm i.d. column packed with 5 um spherical particles of ODS-Hypersil, eluted at 2.0 ml/min with degassed, HPLC-grade MeOH-H_2O 75:25 v/v. Injections of steroids, dissolved in MeOH, were made via a Rheodyne 7125 valve fitted with a 20 ul loop. Detection was at 282 nm x 1.28 AU fsd and peak areas were measure using a Trivector TRIO computing integrator.

RESULTS AND DISCUSSION

Pure cyproterone acetate standard gave a sharp, symmetrical peak on reverse phase analysis on ODS-Hypersil, eluting with MeOH/H_2O (75:25 v/v) with k' 2.0 and (70:30 v/v) with k' 3.4.

Tablets containing 5 mg or 10 mg of cyproterone acetate were extracted with MeOH and analysed by HPLC on ODS-Hypersil using MeOH-H_2O 75:25 v/v as mobile phase. Contents of 100% $\pm$5% (RSD 2.8% for 10 tablets of 10 mg and 2.9% for 10 tablets of 5 mg) indicated good recovery. The method provides a fast and reliable procedure for the assay of tablet batches for clinical use.

Samples of tablets more than 10 years old, stored in the dark at ambient temperature, were available and were examined to determine their content and estimate the effects of this period of storage on the formulated steroid. Batches of 10 tablets at each of the two dose levels (5 mg and 10 mg) were analysed and gave results which conformed well with the requirements, both for content and uniformity (Table 1). There was no evidence for steroid decomposition during the 10 year storage period.

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