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## **THE INFLUENCE OF THE USE OF MULTIPLE DOSES OF DHEA ON THE STEROID PROFILE**

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### **INTRODUCTION**

Dihydroepiandrosterone (DHEA) is produced by the adrenal glands and is one of the most abundant natural occurring hormones in the human body. Serum levels are 20 times higher than any other adrenal hormone. DHEA is known predominantly as a precursor to other hormones, including testosterone and estradiol.

Controlling steroid abuse requires effective means to determine the administration of this group of banned substances. For synthetic anabolic androgenic steroids, the identification of the parent steroid and/or metabolites in urine is evidence that abuse has taken place. For substances that are produced naturally, like DHEA and testosterone, the mere presence of the substance in the urine obviously cannot constitute proof of an offense. For this reason it is important to find other parameters to proof the intake of natural producing steroids.

### **AIM**

The aim of this study was to determine what parameters in the steroid profile can be used to proof the intake of DHEA.

## **MATERIALS AND METHODS**

### **Excretion study**

Two normal caucasian volunteers participated in this study.

Subject 1 was a male, 28 years of age and weighing 82kg.

This subject took capsules containing 25mg DHEA, distributed by Body Chem, South Africa. This product is classified as a nutritional supplement and can be purchased without prescription.

Subject 2 was a male, 50 years of age and weighing 90kg.

This subject took a product XL-2000 from Sportron International, Plano, Texas. This product contains, beside some vitamins, 25mg DHEA per tablet. This product is not available in South Africa but was a gift from Sportron South Africa.

Each subject took 50mg of DHEA in the morning at 08h00 for 12 days.

Urine was collected for a period of 2 days prior to ingestion of DHEA, then for the 12 days during ingestion of DHEA and then for another 3 days after ingestion of DHEA. Urine was collected every day in 3 fractions: 8 - 14h; 14 - 20h and 20 - 08h, 51 samples for each subject.

### **Analysis of samples**

The pH and SG of all samples were measured. Endogenous steroids were quantified by GC/MS (SIM), as routinely done for samples collected for dope analysis. E.coli enzyme was used for hydrolysis at pH 7; so only free and glucuronide conjugates were detected.

## Statistical analysis

- The median, 5% and 95% reference ranges for the endogenous steroids from samples analysed routinely in our laboratory were calculated (n = 760) using Microsoft Excel 5.
- The non-parametric approach with percentiles were used.
- For DHEA the concentrations obtained in January and February 1999 in our laboratory were used.
- Far outside values were determined by adding 3 times the interquartile range to the 75th percentile.

## RESULTS AND DISCUSSION

Urine samples arriving in the laboratory for dope testing are only untimed urine samples and baseline values are not available. The importance of steroid profiling and the use of population based reference ranges were first described by Donike [1,2]. For this reason the samples analysed routinely in our laboratory were used to establish population based reference ranges. These reference ranges were used to evaluate the urinary steroid profile obtained after the intake of multiple doses of DHEA.

The change in urinary concentration of DHEA over time is presented in fig 1. The concentrations rises to above the far outside value for a very short time, mainly in the 08h – 14h samples. After cessation of DHEA intake the concentration drops to normal values within 24 hours.

The concentrations of androsterone (Andro) and ethiocholanolone (Etio) (fig 3 and 4) rise to above the far outside values for the duration of DHEA intake but drops back to normal values within 24 hours after cessation of DHEA intake. This effect is more pronounced for ethiocholanolone. The ratios Etio:Andro are also elevated (fig 9) but only 3 values are above the far outside value. It is interesting to note that this ratio is elevated for a longer time than other ratios and returns to normal only after 48 hours after cessation of DHEA intake.

The concentrations of testosterone (T) and epitestosterone (ET) are also elevated for the duration of DHEA intake with the T slightly more elevated than the ET (fig 5 and 6). Subject 1 has a normal elevated T and ET concentration, with ET more pronounced. The T:ET ratios (fig 2) rise to about 2 times the normal values for both subjects.

The urinary concentrations of 17 $\beta$ -methyl-5 $\alpha$ -androstane-3 $\alpha$ ,17 $\beta$ -diol (5 $\alpha$ -diol) and 17 $\beta$ -methyl-5 $\beta$ -androstane-3 $\alpha$ ,17 $\beta$ -diol (5 $\beta$ -diol) (fig 7 and 8) show the same trend as for Andro and Etio, with almost all the values above the far outside value. This effect is more pronounced for 5 $\beta$ -diol. The ratios of 5 $\beta$ -diol:5 $\alpha$ -diol (fig 10) are also elevated but not significantly. The ratios are more elevated for subject 1 (double the baseline value) than for subject 2 where the ratios are only elevated in some urine samples. These ratios are all elevated for 48 hours after cessation of DHEA intake.

The ratios of Etio:ET and 5 $\beta$ -diol:ET are also elevated but not above the far outside values.

## CONCLUSION

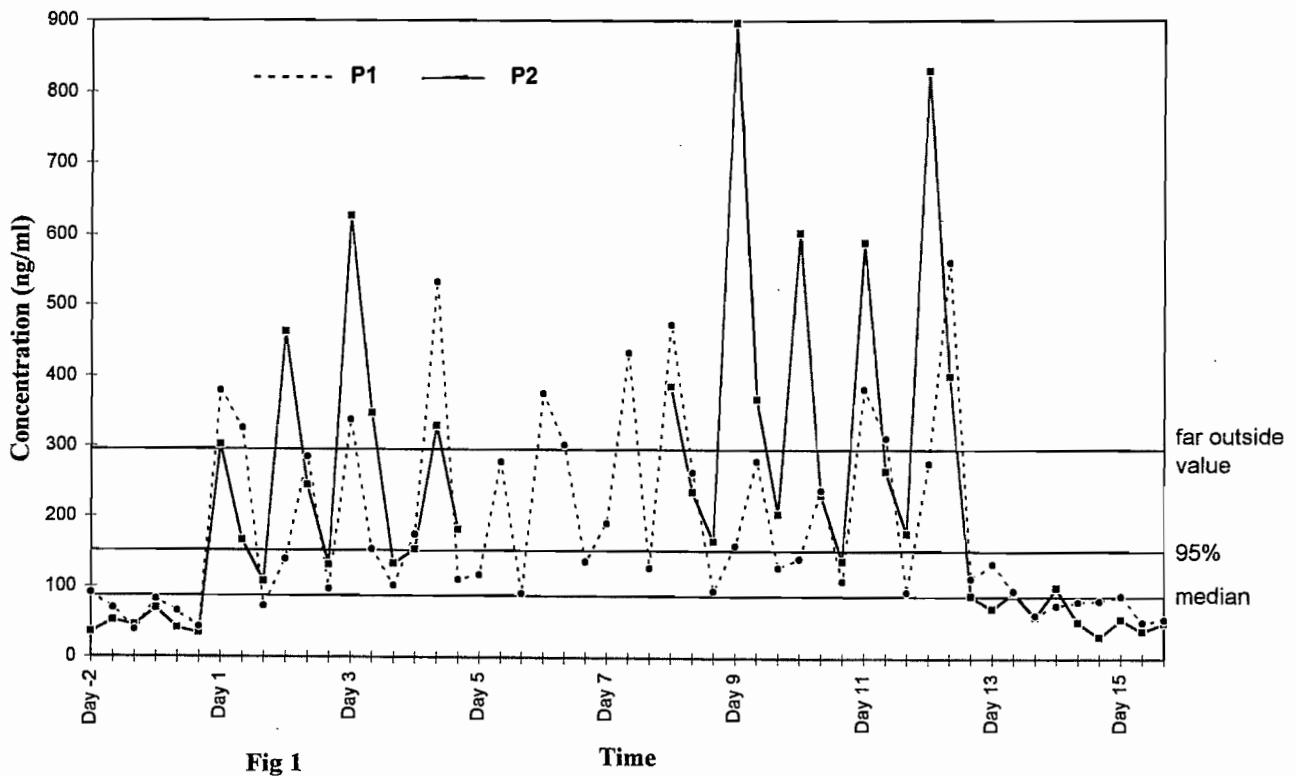
From the results of this pilot study with only 2 subjects it is clear that the half-life of DHEA is too short to detect DHEA abuse. Although the intake of DHEA increases the T levels in urine, this increase is not sufficiently pronounced to be mistaken for testosterone abuse. None of the ratios in the steroid profile is conclusive to prove DHEA intake.

The elevation in the concentrations of Etio and 5 $\beta$ -diol seems to be the main feature after DHEA intake. However, this elevation only leads to a suspicion that DHEA was used and cannot be used to prove the abuse of DHEA. It can finally be concluded that evaluation of the steroid profile cannot be used to prove DHEA abuse.

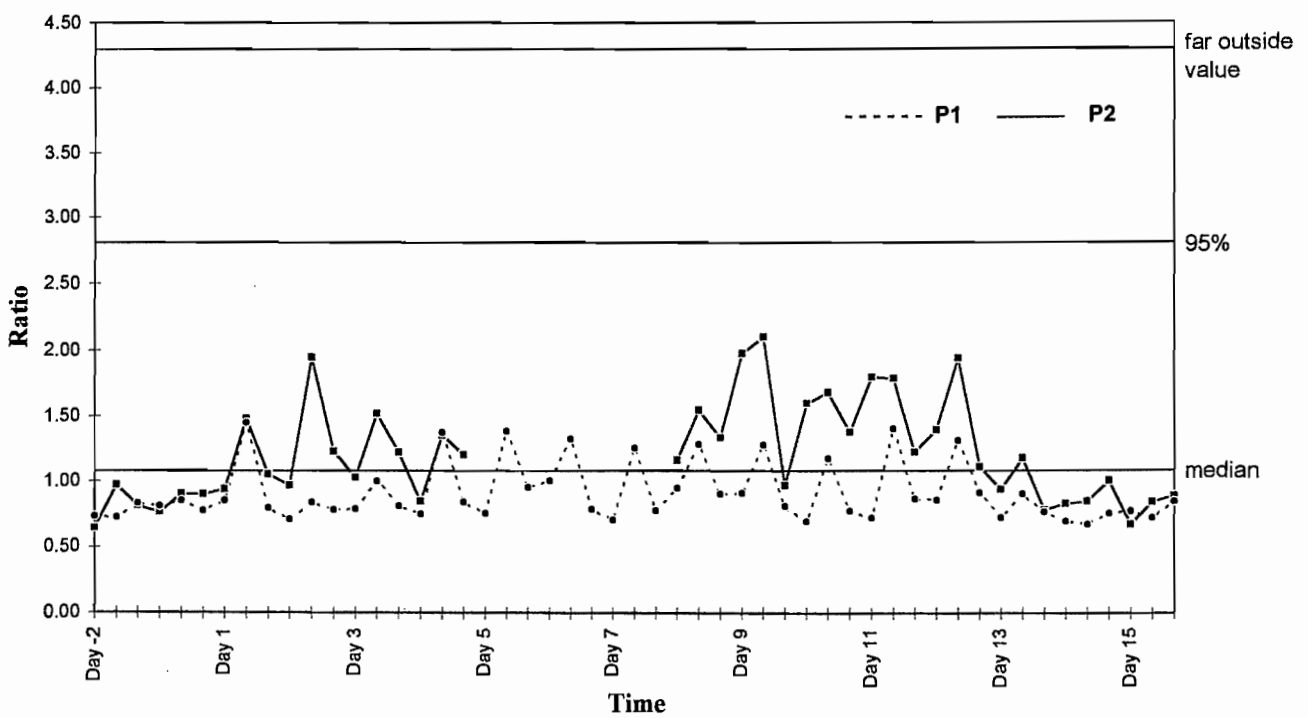
## REFERENCES

1. Donike M. Steroid profiling in Cologne. In M. Donike (Editor), Proceedings of the 10 th Cologne Workshop in Dope Analysis 1992, Sport und Buch Strauß, Köln 1993, p 47.
2. Donike M, Rauth S and Wolansky A. Reference Ranges of Urinary Endogenous Steroids Determined by Gas-Chromatography/Mass Spectrometry. In Dope Analysis 1992, Sport und Buch Strauß, Köln 1993, p 69.

### DHEA



### Testosterone/Epitestosterone



### Androsterone

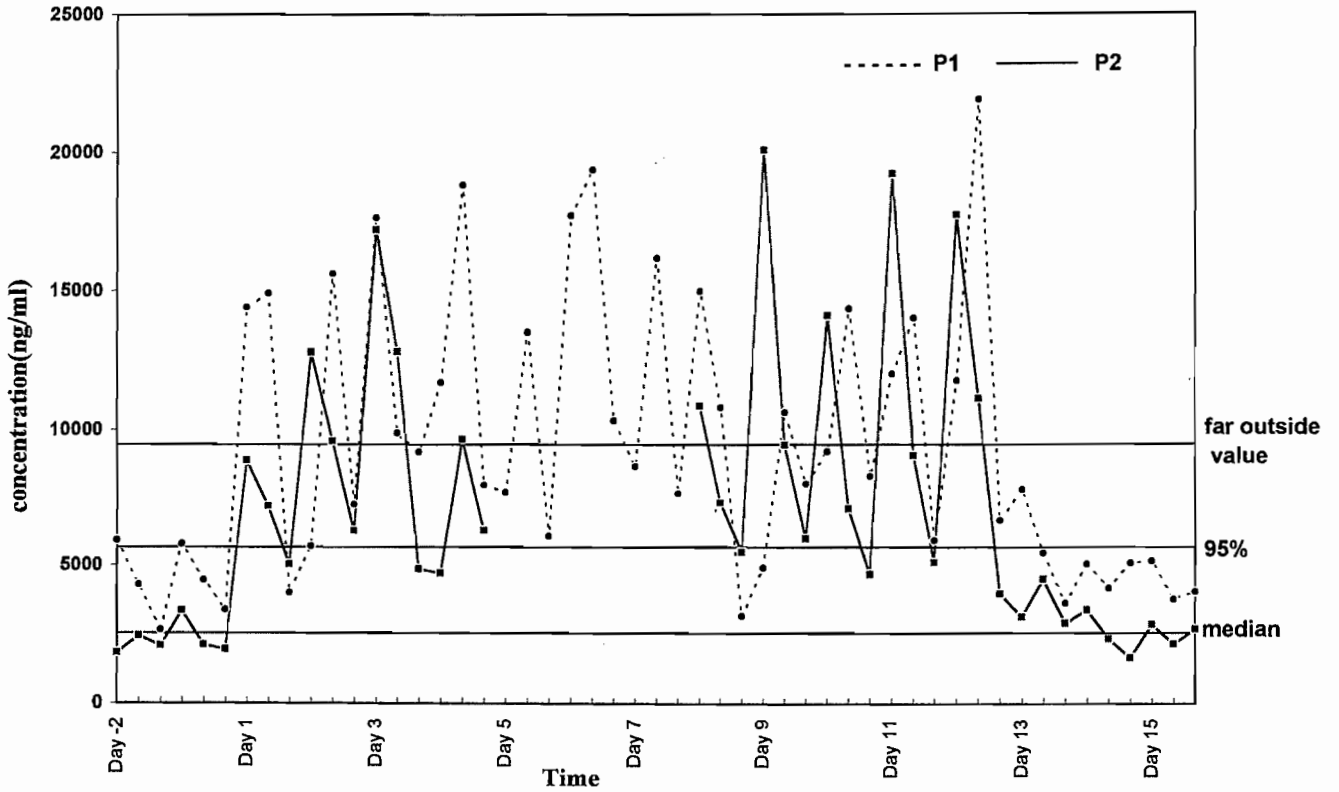


Fig 3

### Ethiocholanolone

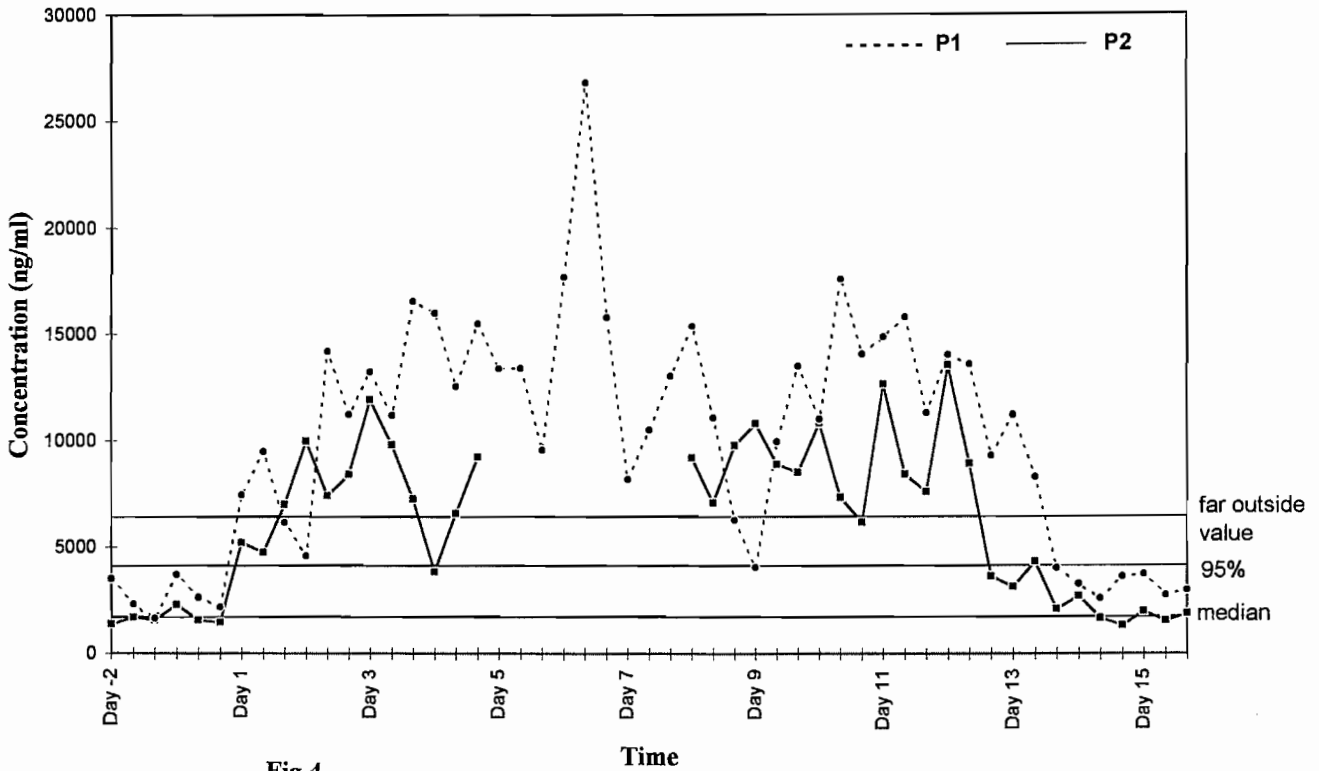
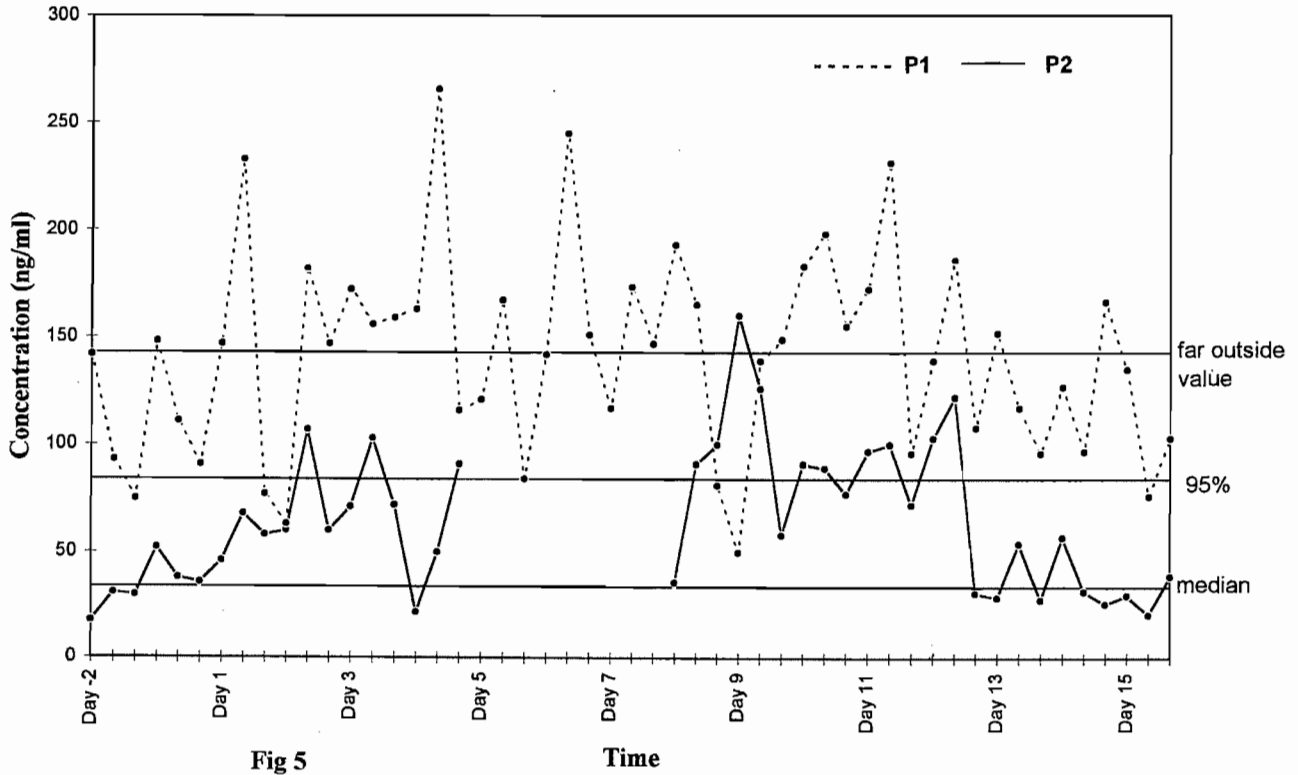


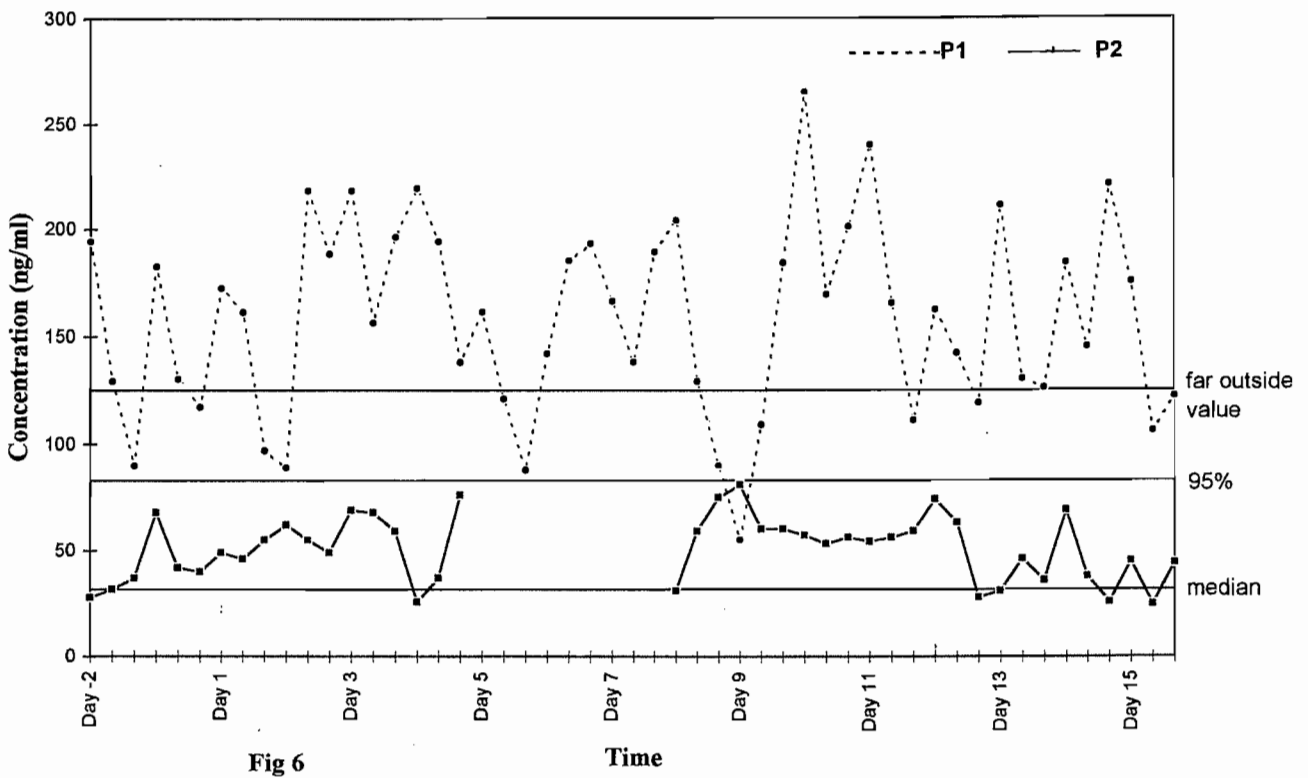
Fig 4



### Testosterone



### Epitestosterone



### 5 $\alpha$ -diol

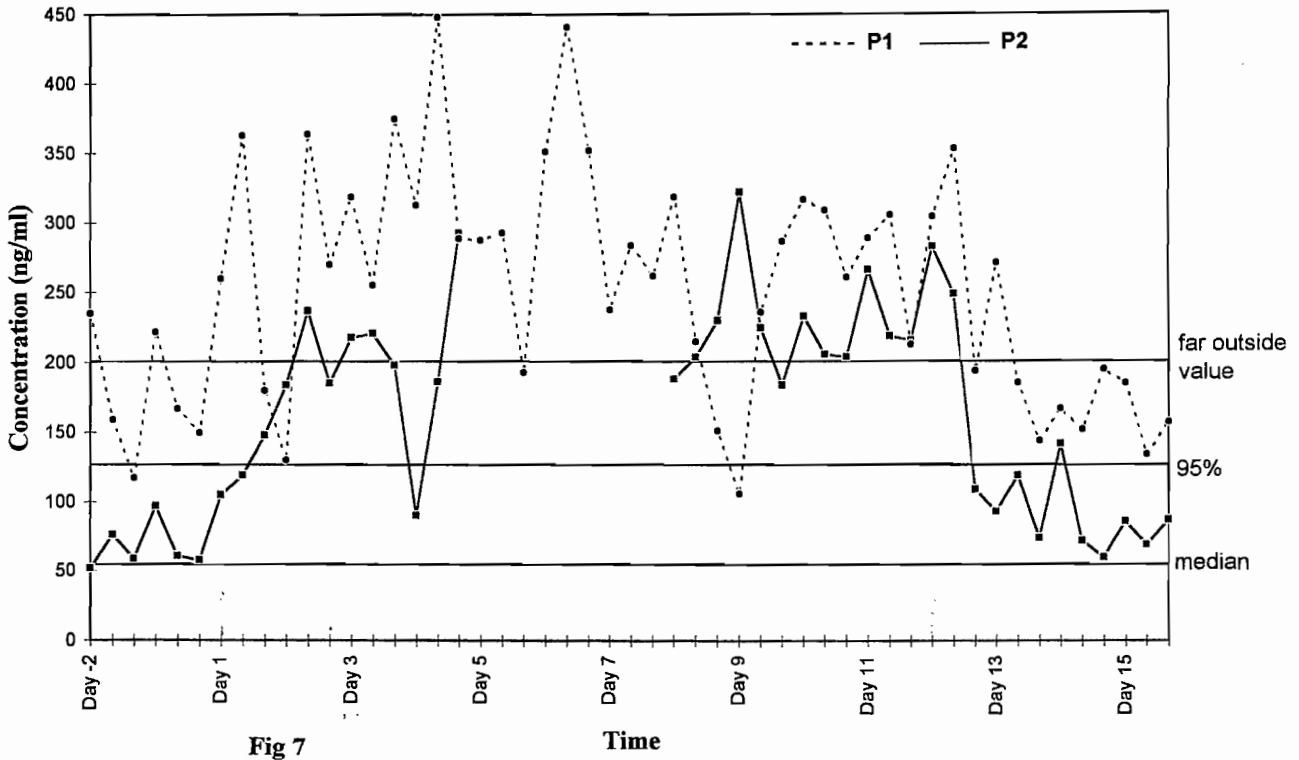


Fig 7

### 5 $\beta$ -diol

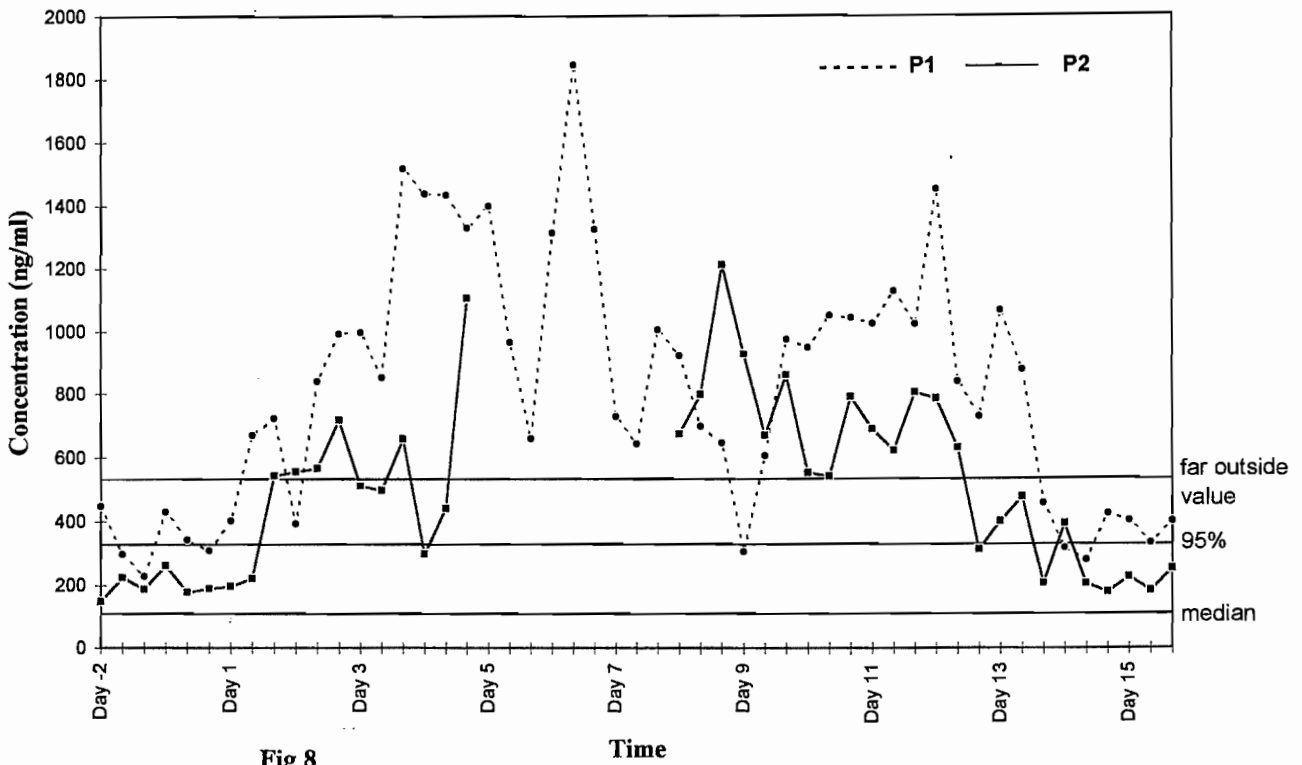


Fig 8

### Ethiocholanolone/Androsterone

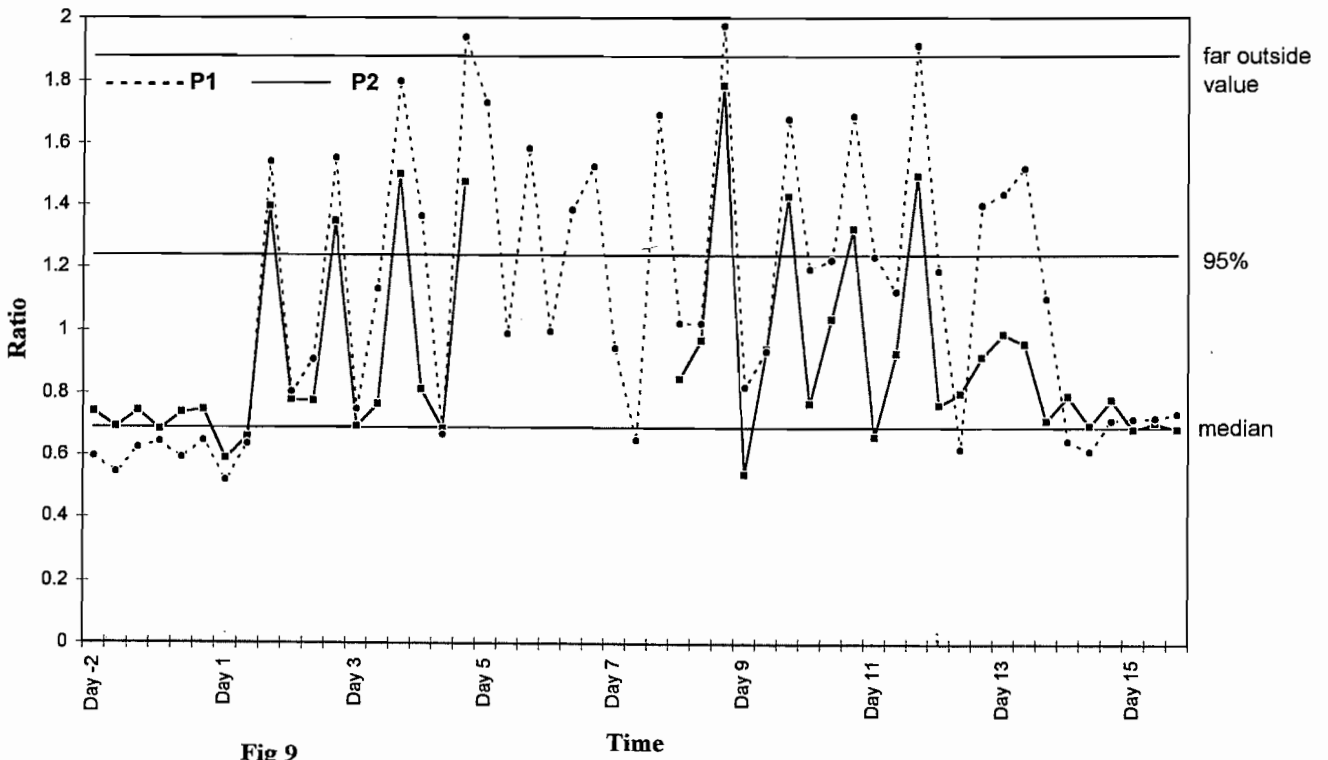


Fig 9

### 5 $\beta$ -diol/5 $\alpha$ -diol

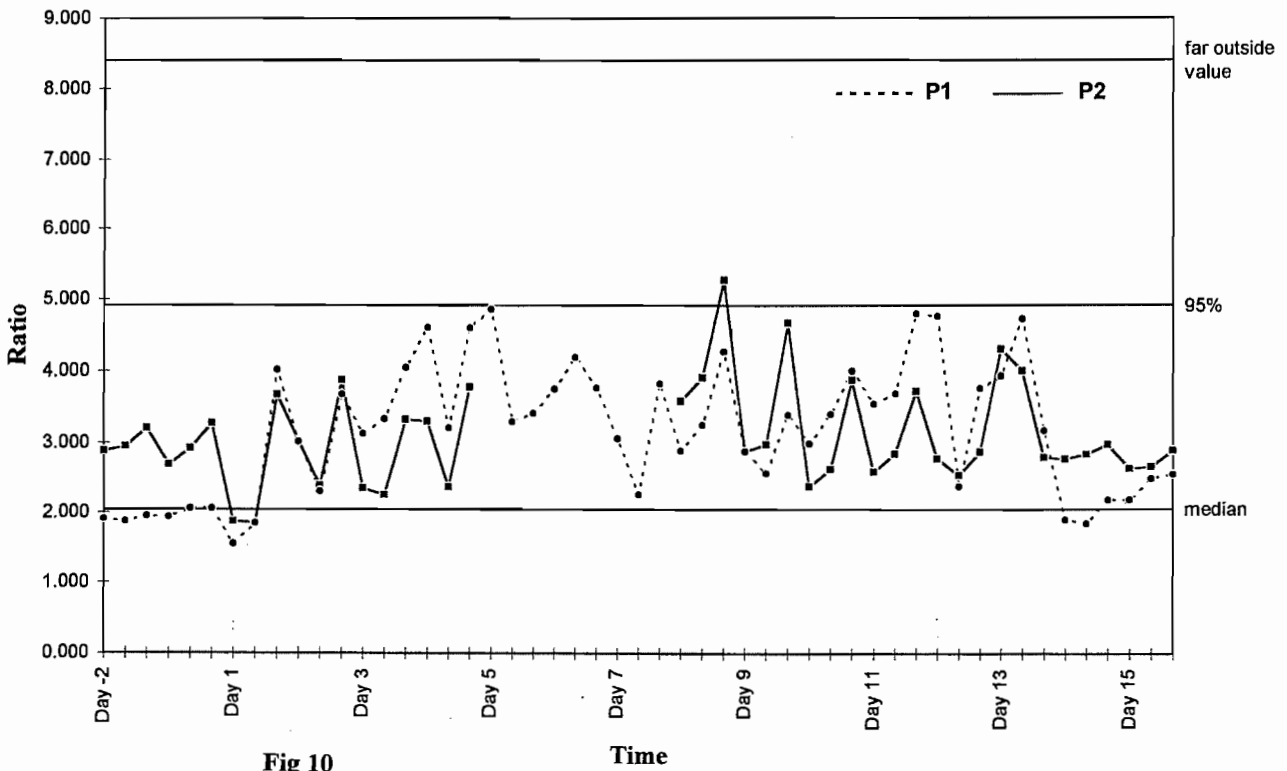


Fig 10