In: Donike, H. Geyer, A. Gotzmann, U. Mareck-Engelke, S. Rauth (eds.)
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The influence of propyphenazone on the excretion of steroids

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Introduction

Propyphenazone belongs structurally to the group of pyrazolone derivatives and therapeutically to NSAIDs (Non-steroidal Anti-Inflammatory Drugs). It has also analgetic effects. The general use is the treatment of fever, pain during influenza or colds and after vaccination. The drug is not prescribed often nowadays, because of more and more severe side-effects. The normal dose is 150-300 mg 1 to 3 times per day. Some cyclists use pharmaceutical combination formulations containing propyphenazone during more day events to suppress pain. Table 1 shows a selection of such formulations, which contains propyphenazone and are available in the Netherlands and Belgium.

Table 1 Pharmaceutical combination formulations containing propyphenazone

name	dose	compounds
the Netherlands		
Saridon®	175 mg	propyphenazone
	50 mg	caffeine
	250 mg	paracetamol
Belgium		
Optalidon®	175 mg	propyphenazone
	25 mg	caffeine

Routine analysis of steroid profiles in our laboratory showed a high correlation between the presence of propyphenazone metabolites and decreased concentrations of testosterone and epitestosterone. This observation prompted us to study the effect of propyphenazone on the excretion of steroids in general and of testosterone and

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epitestosterone in particular.

Experimental

Three male subjects participated in the propyphenazone study. The protocol consisted of a total of 3 days (Table 2). The first day was a 'blank' day and at the second day 3 tablets of Optalidon® were given. The third day was a follow-up day. Urine samples were collected on spontaneous voiding of the bladder. In the obtained urine samples the concentrations of the glucuronides of testosterone (T) and epitestosterone (E) were determined, respectively. The differences were evaluated by the Wilcoxon signed-rank test. The significance was set at 0.1.

Table 2 Protocol of the propyphenazone administration experiment in human volunteers

day	time	sampling	miscellaneous
01	0900 h	urine on spontaneous voiding	start of sampling
02	0900 h	urine on spontaneous voiding	1 tablet Optalidon®
	1100 h		1 tablet Optalidon®
	1330 h		1 tablet Optalidon®
03		urine on spontaneous voiding	
04	0900 h	urine on spontaneous voiding	end of sampling

Results and discussion

The effect of Optalidon® medication on urine parameters was studied. Excretion values were determined per 2 h interval. As the urine samples were not collected on fixed times, the values had to be re-calculated from one or more samples within these 2 h intervals. To minimize the effect of individual variation, the values were expressed as a percent change from baseline (defined as the mean value at the day before the

medication). In the Figures 1 - 3 the mean excretion values of the glucuronides of T and E and the respective T/E ratio are shown. The excretions of T and E indicated a consistent significant difference after Optalidon® administration, compared to the mean value of the blank day. The T/E ratio however, was rather stable. This suggests that Optalidon® medication possibly may have decreased the T and E excretion values. The remark should be made that the significance level was set at 0.1, because of the small number of subjects studied.

Also should be stated, that the observed effect on the T and E excretion values during the laboratory experiment was smaller, than apparently observed in urine samples during routine analysis. The so-called effect of propyphenazone is therefore not equal to the effect observed in the Optalidon® administration experiment. Perhaps more parameters are involved.

The decrease in T and E excretion values could also be caused by a propyphenazone induced inhibition of β-glucuronidase/ arylsulfatase during the hydrolysis of the conjugated steroids. This hypothesis was however not likely, because chemical hydrolysis with methanolic acetic acid also showed a decrease of the T and E excretion values after Optalidon® medication.

Although not clear yet, it should be considered that in combination with Optalidon® medication decreased T and E excretion values can be observed. The interpretation of steroid profiles should therefore at least take into account the possible influence of propyphenazone on steroid excretion values.

References

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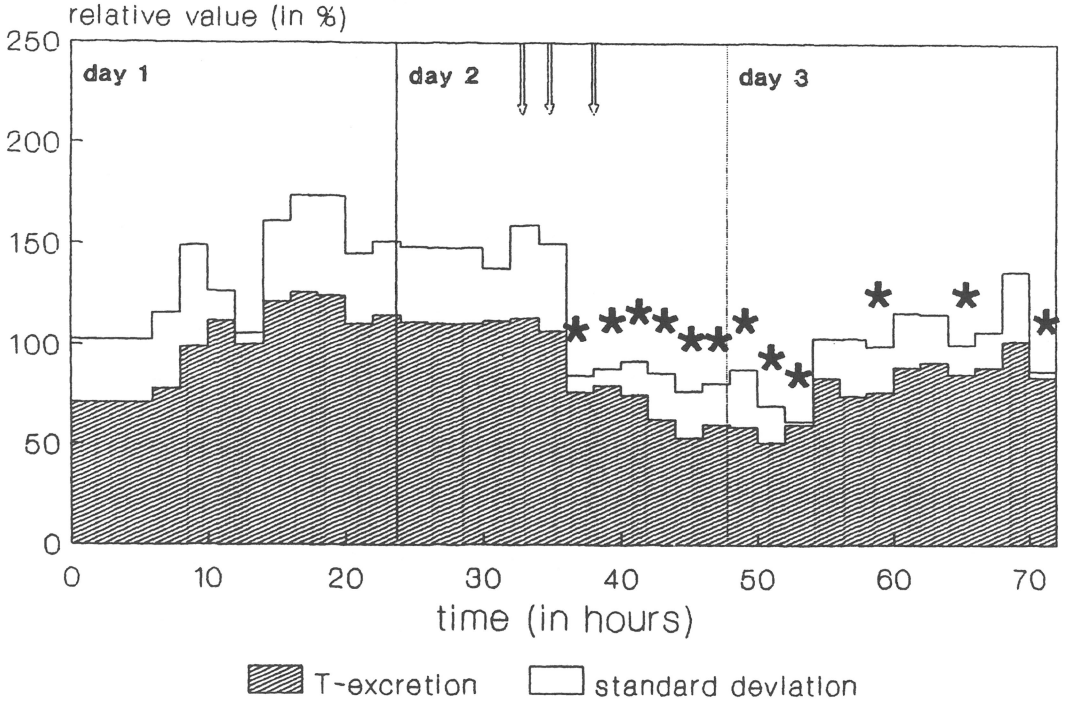

Figure 1: Mean excretion values of the glucuronide of Testosterone during the Optalidon® experiments (normalized on the mean value at the day before the medication) (★ $p < 0.1$)

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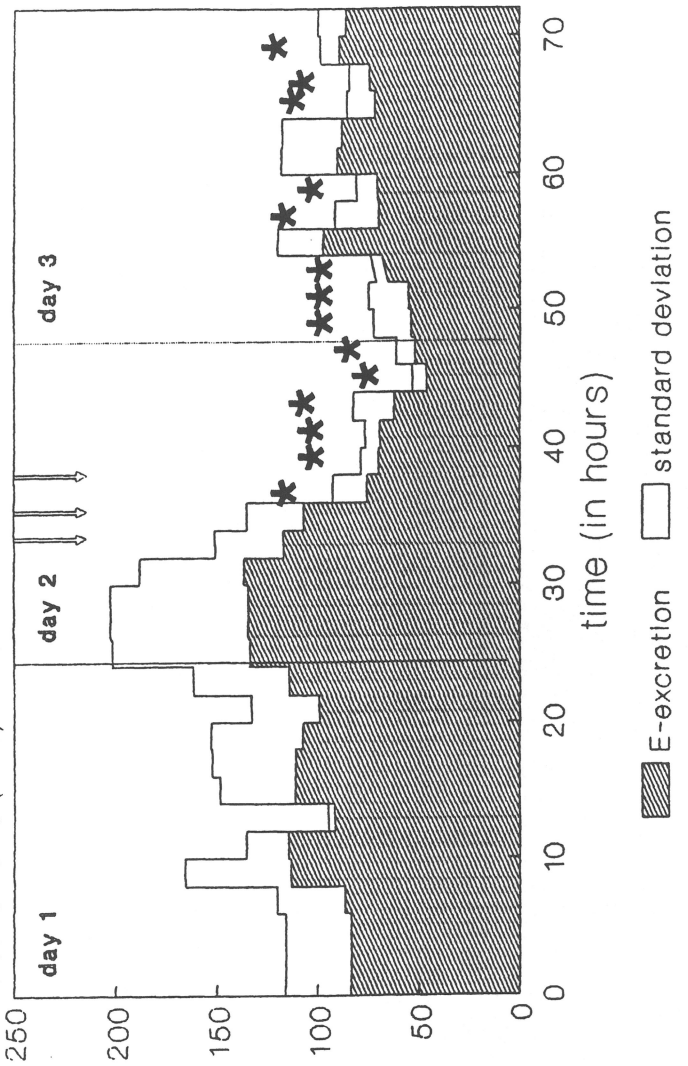

Figure 2: Mean excretion values of the glucuronide of Epitestosterone during the Optalidon® experiments (normalized on the mean value at the day before the medication) (★ $p < 0.1$)

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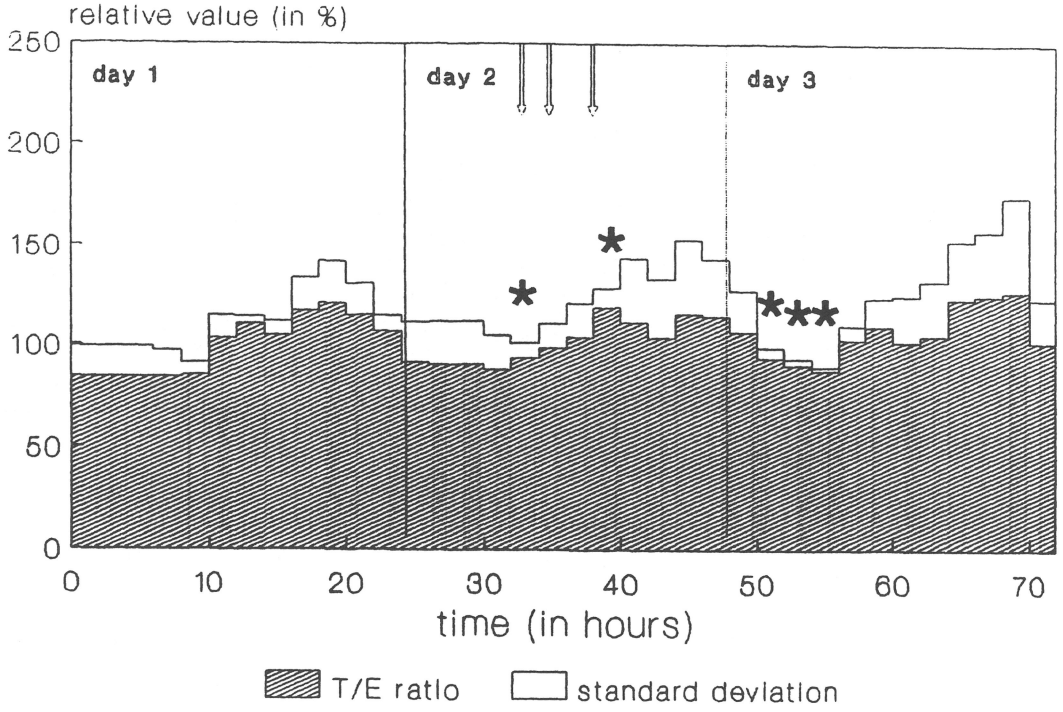

Figure 3: Mean T/E ratio during the Optalidon® experiments (normalized on the mean value at the day before the medication) (★ $p < 0.1$)