

## **PROJECT SUMMARY**

### **“Investigation about the effects and the detection of finasteride, a substance which can be misused as masking agent in doping control”**

**W. Schanzer, H. Geyer** (German Sport University, Cologne, Germany)

Finasteride is an inhibitor of 5-alpha reductase, the enzyme responsible for conversion of testosterone to dihydrotestosterone. It is administered orally in a dose of 5 mg daily for the treatment of benign prostatic hypertrophy. Since 1999 it is also admitted in several countries for the treatment of men with hair loss (androgenetic alopecia) and it seems to become a so called „life style drug“. The recommended dose for the treatment of hair loss is 1 mg/day.

Recent studies with finasteride have shown, that this substance can be misused as a potential masking agent. The application of finasteride may prevent the detection of misuse of anabolic-androgenic steroids like nandrolone, norandrostendione, norandrostenediols, dihydrotestosterone and testosterone. These preliminary results should be confirmed by more extensive studies with several volunteers. If the preliminary results can be confirmed, it should be discussed, if finasteride is added to the prohibited class of masking agents. The second aim of the study is to develop and validate a sensitive and specific method for the detection of finasteride misuse.

## **Investigation about the effects and the detection of finasteride, a substance which can be misused as masking agent in doping control**

### **Results and conclusions**

Finasteride is an inhibitor of 5-alpha reductase and used for the treatment of benign prostatic hypertrophy and androgenetic alopecia. Investigations with finsteride with only one volunteer have shown, that the use of finasteride complicates the detection of the misuse of several anabolic steroids in doping control. To confirm this result and to study the influence of finasteride on the urinary steroidprofile and on the metabolism of anabolic androgenic steroids excretion studies with single oral administrations of 5 mg and 1 mg finasteride were performed with 5 volunteers. Urine samples were collected before and till 8 days after the application and the profiles of endogenous urinary steroids were analysed by GC/MS.

It could be shown, that finasteride led to obvious changes of several steroidprofile parameters. The excretion of 5-alpha-steroids like androsterone, 5 $\alpha$ -androstane-3 $\alpha$ , 17 $\beta$ -diol, allo-tetrahydrocortisol, 11 $\beta$ -hydroxy-androsterone, and dihydrotestosterone decreased, whereas the excretion of the 5 $\beta$ -steroids increased or didn't change. The results were obvious decreases of the ratios between epimeric 5 $\alpha$ -and 5 $\beta$  steroids like e.g. androsterone/ etiocholanolone, 5 $\alpha$ -androstane-3 $\alpha$ , 17 $\beta$ -diol/5 $\beta$ -androstane-3 $\alpha$ , 17 $\beta$ -diol and allo-tetrahydrocortisol/ tetrahydrocortisol. These changes could be detected for more than 8 days both with 5 mg and 1 mg finasteride. The suppression of the excretion of the 5-alpha-steroids showed the same extent for 5 mg and 1 mg finasteride, whereas the increase of the excretion of the 5 $\beta$ -steroids was weaker with 1 mg finasteride compared to 5 mg finasteride. The ratio testosterone/ epitestosterone showed no changes after the application of finasteride and varied within the normal variation.

Further excretion studies with 5 mg finasteride were performed with volunteers, who administered additionally 20  $\mu$ g norandrostendione. It could be shown that under the influence of finasteride the excretion of the 5 $\alpha$ -steroid norandrosterone, the main metabolite of norandrostendione, is suppressed to 20-40% of values without finasteride, whereas the excretion of the 5 $\beta$ -metabolite noretiocholanolone increased under the influence of finasteride up to 400% of the values without finasteride. Based on these results the ratios of norandrosterone/noretiocholanolone changed from values between 1.7-8.4 to values between 0.3-0.7.

The results of the present study show, that the use of finasteride may cause serious problems for the interpretation of steroidprofiles which play an important role in doping control (detection of the misuse of endogenous steroids, longitudinal studies, individualisation of samples, etc.). Furthermore finasteride can complicate or even prevent the detection of 19-norsteroids, which is mainly based on the detection of the their 5-alpha metabolite norandrosterone. These results show that finasteride can be misused as masking agent.

Within this research project a method for the detection of the use of finasteride was developed. As main urinary metabolite a carboxy metabolite of finasteride was identified by LC/MS. This metabolite could be included in an existing screening procedure for doping substances. After a single oral application of 5 mg of finasteride the carboxy metabolite could be detected for 90 hours.

### **Publications and poster presentations**

1) Geyer, H., Gorius, I., Mareck, U., Thevis, M., Schänzer, W.: Investigation about the effects and the detection of finasteride. In: W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck (eds.) Recent advances in doping analysis (13). Sport und Buch Strauß, Köln (2005) accepted for publication

2) Geyer, H., Gorius, I., Mareck, U., Thevis, M., Schänzer, W.: Investigation about the effects and the detection of finasteride. Manfred-Donike-Workshop, 23rd Cologne Workshop on Dope Analysis, Cologne, 2005.