

PROJECT REVIEW

"Identification and synthesis of a new long-term excreted metabolite of metandienone"

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Since midyear 2005 we detect with new mass spectrometric techniques in doping control samples a new unknown metandienone metabolite. First studies indicate that this metabolite can be detected for a longer time period than all other metandienone metabolites. The aim of the study is 1: to identify the structure of this unknown metandienone metabolite, 2: to investigate the excretion kinetics in comparison to other metandienone metabolites, 3: to synthesize reference substances and 4: to implement this substance in existing screening procedures for the detection of doping substances. The analysis of long-term metabolites can improve the fight against doping in the out of competition period in general, because misuse of anabolic steroids can be detected for a longer time.

Results and Conclusions

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Anabolic-androgenic steroids have been one of the most frequently detected drugs in amateur and professional sport. Doping control laboratories have developed numerous assays enabling the determination of administered drugs and/or their metabolic products that allow retrospectives with respect to pharmacokinetics and excretion profiles of steroids and their metabolites.

A new metabolite generated from metandienone has been identified as 17a-methyl-17b-hydroxymethyl-androst-1,4,13-trien-3-one in excretion study urine samples providing a valuable tool for the long-term detection of metandienone abuse by athletes in sports drug testing. The metabolite was characterized using gas chromatography - (tandem) mass spectrometry, liquid chromatography – tandem mass spectrometry and liquid chromatography – high resolution/high accuracy (tandem) mass spectrometry by characteristic fragmentation patterns representing the intact 3-keto-1,4-diene structure in combination with typical fragment ions substantiating the proposed C/D-ring structure of the steroid metabolite. In addition, structure confirmation was obtained by the analysis of excretion study urine specimens obtained after administration of 17-CD₃-labeled Metandienone providing the deuterated analogue to the newly identified metabolite. 17a-Methyl-17b-hydroxymethyl-androst-1,4,13-trien-3-one was determined in Metandienone administration study urine specimens up to 19 days after application of a single dose of 5 mg, hence providing a detection period extended by more than one week compared to commonly employed strategies.

Publications:

- Schanzer W, Geyer H, Fuscholler G, Halatcheva N, Kohler M, Parr MK, Guddat S, Thomas A, Thevis M: Mass spectrometric identification and characterization of a new long-term metabolite of metandienone in human urine. *Rapid Commun Mass Spectrom.* 2006;20(15):2252-8.