PROJECT REVIEW

"Investigations on steroid profile alteration and metabolite excretion of the supplement ingredient Androst-1-ene-3, 17-dione for improvements of analytical result interpretation"

M.K. Parr, **W. Schanzer** (German Sport University, Cologne, Germany)

As per list of the World Anti-Doping Agency (WADA) 1-Androstenedione is classified as "exogenous anabolic androgenic steroid" and is therefore prohibited in sports. Recently it appears as ingredient of products of the dietary supplement market as so-called prohormone of 1-Testosterone.

Only very limited information is available on its effects and metabolism. It is very likely that the endogenous steroids 17-hydroxy-5-androstane-3-one (5-DHT), 3-hydroxy-5-androstane-17-one (Androsterone), and 5-androstane-3,17-diol occur as metabolites. Altered steroid profiles are therefore expected, especially the ratios of 5/5-androstane-3,17-diol (ADIOL/BDIOL) and androsterone/etiocholanolone (AND/ETIO) may be influenced. A concentration of 5-DHT>21 ng/mL (adjusted for specific gravity) together with ADIOL/BDIOL>1.5, AND/ETIO>2.9, DHT/ETIO>8.2 and DHT/EpiT>0.73 is considered as indicative for the administration of 5-DHT in males. Thus, a potential misinterpretation of the results obtained after 1-Androstenedione administration has to be taken into account.

Thus, the project aims in monitoring the influences on urinary steroid profiles. An identification of other urinary metabolites as well as the evaluation of their time courses will be part of the project as well.

“Investigation on Steroid Profile Alteration and Metabolite Excretion of the Supplement Ingredient Androst-1-ene-3,17-dione for Improvements of Analytical - Result Interpretation”

M.K. Parr, W. Schanzer (German Sport University Cologne, Germany)

Results and conclusion

New analogs of androgens that had never been available as approved drugs are marketed as “dietary supplement” recently. They are mainly advertised to promote muscle mass and are considered by the governmental authorities in various countries, as well as by the World Anti-doping Agency for sport, as being pharmacologically and/or chemically related to anabolic steroids.

Recently so-called prohormones of 1-testosterone (17β-hydroxy-5α-androst-1-en-3-one), namely 1-androstenedione (5α-androst-1-ene-3,17-dione, 1-AD) and 1-androstenediol (5α-androst-1-ene-3β,17β-diol) are advertised as well. Only very limited information is available on their effects and metabolism.

Within this project the urinary metabolism of 1-androstenedione was investigated and the main metabolites were monitored following administration of a single oral dose of 50 mg to six male volunteers. 1-Testosterone, 3α-hydroxy-5α-androst-1-en-17-one (1-DHA), 3β-hydroxy-5α-androst-1-en-17-one (1-DHEA), 5α-androst-1-ene-3α,17β- and -3β,17β-diol were detected besides the parent compound and two more metabolites (up to now not finally identified but most likely C-18 and C-19 hydroxylated 5α-androst-1-ene-3,17-diones). Additionally, common urinary steroid profile ratios were altered after the administration. Especially the ratios of androsterone/etiocholanolone and 5α-/5β-androstane-3α,17β-diol and the excretion rate of androsterone were increased for about 2 days post administration. 1-DHA appears to be suitable for the long-term detection of the steroid (ab-)use, as this characteristic metabolite was detectable in screening up to ten days after single administration. It was synthesized within this project and characterized by MS and NMR.

For biological characterization 1-androstenedione, and its metabolites 1-testosterone, 1-DHA, and 1-DHEA were tested in a yeast androgen assay as measure of the androgenic potential. 1-AD displayed androgenic affects itself (1/10 as active as 5α-dihydrotestosterone (DHT)) and thus may not be classified as prohormone but as active hormone. However, its metabolite 1-testosterone is able to transactivate androgen receptor driven reporter genes in the yeast androgen screen with a comparable potency as the reference androgen DHT. The two other tested compounds, 1-DHA and 1-DHEA, were about 1/100 as active as DHT.