PROJECT REVIEW

"Differentiation between the administration of the aromatase inhibitor Androstatrienedione, and the anabolic androgenic steroids Boldione and Boldenone"

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As per list of the World Anti-Doping Agency (WADA) 2009 Boldenone and Boldione are explicitly listed in group S1 "anabolic androgenic steroids", and are therefore prohibited in sports, while Androsta-1,4,6-triene-3,17-dione is classified as aromatase inhibitor (class S4. Hormone Antagonists and Modulators, particularised class S4.1. Aromatase Inhibitors). All these three substances are reported to be excreted as Boldenone and/or Boldenone metabolite in the urine. As class S1 substances are considered as "Non-Specified Substances" while class S4.1. substances are judged as "Specified Substances" the assignment to the administered substances is particularly important for the valuation of the adverse analytical finding. Thus, the project aims to investigate the urinary metabolism and pharmacokinetics using mass spectrometric analyses. Isotope ratio mass spectrometry (GC-C-IRMS) will be applied to identify origin of Testosterone and other endogenously occuring steroids. Based on the analytical data criteria to trace the administered substance have to be established.

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Results and Conclusion

As per list of the World Anti-Doping Agency (WADA) boldenone (BOL) is explicitly listed in group S1.1 "Anabolic Androgenic Steroids", and is therefore prohibited in sports, while androsta-1,4,6-triene-3,17-dione (ATD) is classified as aromatase inhibitor (class S4. Hormone and Metabolic Modulators, particularized class S4.1. Aromatase Inhibitors). Both substances are reported to be partially excreted as boldenone and/or boldenone metabolite in the urine.

As class S1 substances are considered as "Non-Specified Substances" while class S4.1. substances are judged as "Specified Substances" the assignment to the administered substances is particularly important for the valuation of the adverse analytical finding. Thus, the urinary metabolism and pharmacokinetics of ATD and BOLD were studied.

Following oral administration of BOLD (50 mg, n=6) 17β-hydroxy-5β-androst-1-en-3-one (BM1) and 3α-hydroxy-5β-androst-1-en-17-one (BM2) were detected as main metabolites besides the parent compound. Additionally lots of other phase-I metabolites together with traces of ATD were detected as metabolites.

Following the administration of ATD (50 mg p.o., n=6) major amounts were excreted as parent compound ATD and 17β-hydroxyandrosta-1,4,6-trien-3-one (17OHAT). As minor metabolites BOLD and other reduction products were detected.

Furthermore influences on the urinary steroid profiles were monitored. None of the classical steroid profile ratios showed a significant alteration after administration of either compound.

The results suggest a ratio of ATD/BM1 and 17OHAT/BM1 as indicators for an administration of ATD. However, for proposal of a cut-off limit further experiments are needed with longer sample collection windows and multiple dose administration.