PROJECT REVIEW

"A-Ring hydroxylation as metabolic pathway for long term detection of steroids"

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The anabolic androgenic steroids (AAS) are prohibited in sports. They are included in the 2017 list of the World Anti-Doping Agency (WADA) as class S1. In the last years the anabolic agents accounted for most of the adverse analytical findings (AAF) in doping control (e.g. in 2015 50% of all ADAMS reported AAF). AAS undergo extensive metabolization, thus, urinary detection of a prohibited administration is mainly based on the detection of metabolites. As some steroids also occur naturally in the body, their uncoverage generally uses specific ratios, such as testosterone/epitestosterone (T/EpiT), androsterone/etiocholanolone (And/Etio), And/T, and 5α-/5β-androstane-3α,17β-diol (Adiol/Bdiol), that proved to be very stable in humans. Confirmation of the results generally require isotope ratio mass spectrometry. As confirmation is very elaborate and cost intense some minor metabolites came into the focus of anti-doping scientists to increase the efficiency of screening procedures. For the improved detection of an exogenous administration of androstenedione the usefulness of the A- or B-ring hydroxylated metabolites 4-hydroxy-androstenedione, 6z-hydroxy-androstenedione was reported. As already published 2β- and 15β-hydroxylation also occurs in testosterone metabolism with ~10% and 4% of the rate of the most dominant hepatic microsomal 6β-hydroxylation. Furthermore, it was demonstrated that the use of 2- and 4-hydroxyandrostenedione may serve as long term marker of an androstenedione administration. The metabolic generation could be confirmed by in-vitro experiments upon incubation with CYP1A2 and CYP1B1. No reports on the metabolic hydroxylation of androgens by CYP1A2 or by CYP1B1 are found in literature so far. The objective of the project is to further investigate the suitability of A-ring hydroxylation for long-term detection of endogenously occurring androgens and to extent the preliminary investigations to other prohibited steroids.