PROJECT REVIEW

"Improving detection of the confounding factor dutasteride"

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The 5α-reductase enzyme system is involved in the metabolism of endogenous and exogenous steroids. The substrates are the C19/C21 steroids with a keto group at the carbon 3 and a double bond between carbons 4 and 5. The reaction mechanism is complex and involves the binding of a reduced pyridine nucleotide cofactor to the enzyme followed by the substrate.

The modulation of the 5α-reductase activity by 4-azasteroids is used in therapy for the treatment of benign prostatic hyperplasia or androgenic alopecia. In the anti-doping field, the possibility to use the 4-aza-steroids (finasteride and dutasteride) to manipulate the steroid excretion profiles and, consequently, to mask the abuse of both pseudoendogenous and exogenous steroids was demonstrated. From 2005 to 2009, this class of compounds was included in the WADA list in the section S5 "Diuretics and other Masking agents"; whereas since 2014 the 5α-reductase inhibitors are included in the Technical Document TDEAAS "Endogenous Anabolic Androgenic Steroids Measurement and Reporting" as confounding factor. Indeed, the administration of these agents leads to a decrease of the 5α-steroids with a consequent alteration of the ratios between androsterone and etiocholanolone; 5α-androstane-3α,17β-diol and 5β-androstane-3α,17β-diol; and androsterone and testosterone.

Different analytical procedures are reported in literature to determine finasteride in biological fluids, whereas for dutasteride only determinations in blood samples are reported due to its pharmacokinetics properties.

The aim of this project is to select the most appropriate analytical strategy and matrix to detect dutasteride during doping control test in order to avoid the risk to give uncorrected results.